Trauma and Stressor-Related Disorders

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Introduction

This chapter focuses on gender differences in trauma exposure and the development of posttraumatic sequelae over the life course. First, we review the prevalence of trauma exposure and posttraumatic sequelae with particular attention to comorbidity and disability or impairment. Second, we review psychobiological processes that explain risk for various types of posttraumatic sequelae with a focus on gender and comorbidity. Third, we review the DSM-5 diagnostic criteria for various disorders associated with trauma exposure. Fourth, we review the best available instruments designed to assess these disorders. Fifth, we review the current best practices for treatment of these conditions including psychopharmacology, psychotherapy, and combined approaches designed to treat comorbid conditions. We conclude that despite a large body of research documenting gender differences in trauma exposure and trauma-related disorders much work remains to be done in this area.

Epidemiology

Exposures

Potentially traumatic event (PTE) exposure is common with 60–90 % of adults worldwide reporting exposure to at least one PTE during their lifetime (e.g., Bohnert and Breslau 2011; Kessler et al. 1995; Perkonigg et al. 2000; Resnick et al. 1993). PTEs include interpersonal traumas such as rape, mugging, and physical assault as well as non-interpersonal traumas such as flood, fire, and motor vehicle accidents.

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PTEs also include witnessing death and injury to others and learning of the violent death or injury of a loved one. A meta-analysis examining gender differences in trauma exposure and posttraumatic stress disorder (PTSD) found that men are slightly more likely to report exposure to any PTE compared to women (Tolin and Foa 2006). However, exposure to specific types of PTSD varies greatly by gender.

Interpersonal PTEs

Interpersonal violence occurs over the life course, but it is especially common among children, adolescents, and young adults (e.g., Kilpatrick et al. 1992). For example, nearly 1 in 4 children in the United States has experienced physical, sexual, or emotional abuse (Finkelhor and Jones 2006), and comparable rates have been observed globally (Finkelhor 1994). Interpersonal trauma exposure also differs by gender such that girls and women are more likely to experience interpersonal violence such as sexual assault and childhood sexual abuse compared to boys and men (Kessler et al. 1995; Tolin and Foa 2006). For example, two meta-analyses of international studies of child sexual abuse (CSA) suggest that, on average, slightly less than 10 % of men reported CSA while 10–20 % of women reported CSA prior to age 18 (Finkelhor 1994; Pereda et al. 2009). In the United States, 1 in 5 women and 1 in 71 men have experienced a lifetime rape, defined as attempted or completed forced penetration or drug/alcohol facilitated penetration (Black et al. 2011). Approximately 1 in 3 US women and more than 1 in 4 US men (28.2 %) have experienced physical violence by an intimate partner (Black et al. 2011). These rates are consistent with those observed in other US samples (Walsh et al. 2015) and in other developed countries including Australia (Rees et al. 2011); however, the prevalence of violence exposure is considerably higher among women in developing and war-ravaged nations (Heise et al. 1994). For example, World Health Organization data from women aged 15–49 in multiple countries found that 15–71 % of ever-partnered women have experienced rape by an intimate partner and 5–65 % of women reported experiencing physical or sexual violence since age 15 by a non-partner (World Health Organization 2013). Pregnancy is also a period of potentially increased risk for violence exposure among women, with 3–32 % of women worldwide reporting abuse during the peripartum period (Campbell et al. 2004).

Non-interpersonal PTEs

In a nationally representative US survey, the most commonly reported PTEs included non-interpersonal violence such as the unexpected death of a loved one (25 %), serious illness, accident, or injury to a loved one (21 %), and indirect exposure to terrorism (e.g., watching the events of 9/11 unfold on television; 22 %) (Bohnert and Breslau 2011). In the same survey, 17–30 % of trauma-exposed persons reported experiencing a life-threatening accident and 16–25 % reported experiencing a natural disaster (Pietrzak et al. 2011). Numerous studies suggest that men are more likely than women to experience accidents, natural disasters or fires, witnessing death or injury, and combat or war (Kessler et al. 1995; Tolin and Foa 2006).

Outcomes

Posttraumatic Sequelae

Although stress disorder (PTSD) is the most commonly studied outcome of trauma exposure, most persons exposed to PTEs do not develop PTSD (Bonanno 2005). Indeed, despite the fact that nearly everyone will be exposed to at least one PTE during his or her lifetime (e.g., Bohnert and Breslau 2011), estimated lifetime rates of PTSD range from 4 to 14 % in the United States (Breslau 2002; Roberts et al. 2011). Globally, the prevalence of PTSD is relatively consistent, although higher prevalence of PTSD has been observed in countries with greater exposure to war and torture (Steel et al. 2009). Among US women and men, rape and combat exposure, respectively, are the PTEs associated with the highest conditional probability of developing PTSD (Kessler et al. 1995). Despite the fact that men are more likely to experience any PTE, women are more likely to develop PTSD once exposed to a PTE (Breslau 2002; Breslau and Anthony 2007; Tolin and Foa 2006). Indeed, women are twice as likely to develop PTSD when compared to men (Kessler et al. 1995), a finding that may relate to women's increased risk for sexual violence compared to men (Cortina and Kubiak 2006). Among women only, exposure to assaultive violence has been shown to both increase risk for PTSD both immediately as well as when exposed to later non-assaultive violence (Breslau and Anthony 2007).

Comorbidity

Among those persons who meet diagnostic criteria for lifetime PTSD following a PTE, the vast majority have significantly elevated risks for other lifetime disorders (Kessler et al. 1995; for review see Breslau 2002; Koenen et al. 2008a). Trauma-exposed persons with PTSD consistently have been found to have higher risk for suicide as well as anxiety, mood, and substance use disorders compared to those without PTSD (Breslau et al. 1997; Breslau 2002; Blanco et al. 2013; Kessler 2000). Other psychopathologies have been associated with trauma exposure and/or the development of PTSD including major depression (Cuijpers and Smit 2002; Cuijpers et al. 2013), suicidality (van Spijker et al. 2011), personality disorders (Walsh et al. under review), and substance use disorders (Rehm et al. 2009). In one study, the risk of suicidal ideation was five times higher for those with PTSD compared to those without (Kessler 2000). While PTSD and disorders like depression may share similar symptoms, PTSD may be a causal factor for other psychiatric and physical disorders, contribute to the severity of the comorbid conditions, or share common antecedents or vulnerabilities with the comorbidities (Breslau 2009; Koenen et al. 2008a; McLeod et al. 2001). Physical conditions associated with PTSD include increased chronic physical pain and somatization, cardiovascular conditions, autoimmune disorders, impaired immunity, and obesity (for review, see Qureshi 2009).

Significant gender differences also exist in patterns of comorbidity. For example, women with PTSD are more likely than men with PTSD to meet criteria for another anxiety disorder like Panic Disorder (e.g., 12.6 % versus 7.3 %; Kessler et al. 1995), while men with PTSD are more likely than women with PTSD to meet criteria for a substance use disorder (51.9 % vs. 27.9 % for AUD; 34.5 % vs. 26.9 % for drug use disorder) and

conduct disorder (43.3 % vs. 15.4 %) (Kessler et al. 1995). In a study of women only, the PTSD comorbidity with the highest lifetime prevalence was major depression, although women who developed PTSD were at increased risk for both major depression and AUD (Breslau et al. 1997).

Disability and Impairment

Beyond the development of psychiatric conditions, trauma exposure and PTSD also have been associated with significant functional impairment related to physical and psychiatric comorbidities as well as the chronicity of PTSD symptoms. Adverse consequences throughout the life course include increased risk for poor school performance, work impairment such as absenteeism (estimated at over 3.5 days of work missed per month due to PTSD), and unemployment (Kessler 2000). Other psychosocial impacts include marital instability and parenting challenges (Rodriguez et al. 2012; Kessler 2000). Given that PTSD has been found to persist beyond 2 years in about one-third of cases, the disease burden should not be neglected (Breslau 2009; Kessler et al. 1995). Female gender is a risk factor for chronicity of PTSD (Breslau and Davis 1992). Further, in estimating disease burden, resilience theories may be useful for public health planning and treatment. Studies of symptom trajectories following trauma exposure indicate that persons may experience varying levels of symptom severity over time in patterns that indicate, for example, recovery, chronic dysfunction, or relapsing/remitting (Norris et al. 2009). While a single disorder is associated with substantial functional impairment, comorbidity is associated with even greater costs to the individual and society. Thus, understanding how trauma exposure may give rise to or complicate this host of negative outcomes can improve existing prevention and intervention programs and potentially ameliorate the heavy social and economic burden of trauma exposure and related sequelae.

Psychobiology

A number of psychobiological factors may be important to consider the relationship between trauma exposure and posttraumatic sequelae including genetics, neural circuitry, and psychological phenomena.

Genetics

Genetic factors influence who is trauma exposed (e.g., Sartor et al. 2012) and who develops posttraumatic sequelae (e.g., Sartor et al. 2011). For example, twin studies suggest that 47–60 % of the variance in trauma exposure can be attributed to additive genetic factors (Lyons et al. 1993; Sartor et al. 2012), while 30–70 % of the variance in PTSD can be accounted for by genetic factors (Bailey et al. 2010; Sartor et al. 2011; Stein et al. 2002a; True et al. 1993). Heritability estimates for MDD range from 27 to 40 % (Kendler et al. 2006; Lyons et al. 1998; True et al. 1993; Sartor et al. 2012) while heritability estimates for alcohol dependence range from

55 to 71 % (Young-Wolff et al. 2012; Sartor et al. 2011; Ystrom et al. 2011). The genetic correlation between PTSD and MDD ranges from .77 (Koenen et al. 2008a) to 1.0 in one recent sample (Sartor et al. 2012) while the genetic correlation between PTSD and alcohol dependence has been estimated to be as high as .54 (Sartor et al. 2011). Overall, findings suggest that genetic heritability plays an important role in a range of common outcomes associated with PTE exposure, and some of the heritable influences on trauma exposure and related disorders may be shared.

Gene by environment (G×E) studies provide important information about the specific genetic variants that are associated with PTSD, MDD, suicidality, and substance use disorders. G x E studies are particularly well-suited to address genetic questions about PTSD as it is a phenotype that requires exposure to an environmental stressor (Koenen et al. 2009; Koenen et al. 2008b). Recent reviews of the G×E literature relating to PTSD have highlighted interactions between trauma exposure, particularly childhood abuse, and genes involved in the dopaminergic, serotonergic, and neuroendocrine systems (Cornelis et al. 2010; Nugent et al. 2008; Skelton et al. 2012) including the dopamine receptor (D2) and the dopamine transporter (DAT) (e.g., Drury et al. 2009; Segman et al. 2002), the *5-HTTLPR* polymorphism in the promoter region of the serotonin transporter gene (*SLC6A4*) (e.g., Wang et al. 2011; Xie et al. 2009), and *FKBP5*, a regulator of glucocorticoid receptor sensitivity that is involved in HPA axis stress reactivity (Binder et al. 2008; Mehta et al. 2012; Sarapas et al. 2011; for review see Yehuda et al. 2011; Xie et al. 2010). Many of the same genes have been shown to interact with trauma exposure to predict MDD, suicidality, and substance use disorders. For example, polymorphisms in *5-HTTLPR* (Grabe et al. 2012), brain-derived neurotrophic factor (BDNF; Tsai et al. 2003), and proinflammatory cytokine interleukin-18 (IL-18; Haastrup et al. 2012) have been linked to the development of MDD. Similarly, *D2, DAT*, and *5-HTTLPR* have been associated with alcohol dependence (for review see Dick et al. 2003), and 5-HTTLPR has been associated with risk for suicide (Roy et al. 2010). In addition to these associations, sex-specific differences have been noted in a G x E association between *GABRA2* genotype and environmental stressors on alcohol dependence such that men with the risk genotype who had more positive life events were less susceptible to alcohol dependence (Perry et al. 2013).

In addition to family/twin and candidate gene studies, other genetic methods are increasingly being used to study associations between genetics and the development of psychopathology among trauma victims. Genome-wide association studies (GWAS) have been employed to compare DNA markers on the genome in diseased persons as compared to persons free of symptoms of that disorder. Positive results have included an association between PTSD and the retinoid-related orphan receptor alpha (RORA) gene (Logue et al. 2013) and the Tolloid-Like 1 gene (*TLL1*; Xie et al. 2013). Furthermore, in women, a novel positive association has been observed between PTSD and the RNA gene, lincRNA *AC068718.1* (Guffanti et al. 2013) as well as the pituitary adenylate cyclase-activating polypeptide (PACAP) and PAC1 receptor, which broadly regulate the cellular stress response (Ressler et al. 2011). Although some studies have failed to support the PACAP finding (Chang et al. 2011), other replications have garnered support for this association (Uddin et al. 2013). With

regard to substance use disorders, GWAS studies have confirmed associations between alcohol dependence and *ADH1B* and *ADH1C*, while identifying novel risk loci on chromosomes 4 and 2 and population-specific markers on chromosomes 5, 9, and 19 (Gelernter et al. 2014).

Epigenetic mechanisms, which are heritable changes in gene expression or functionality that do not involve changes to the underlying DNA sequence, also may partially explain the development of negative sequelae among trauma-exposed persons. DNA methylation, which involves the addition of a methyl group to the 5 position of the cytosine pyrimidine ring or the number 6 nitrogen of the adenine purine ring, has been the most widely studied with regard to trauma exposure and posttraumatic sequelae. For example, animals exposed to a psychosocial stressor evidence increased DNA methylation in the hippocampus (Chertkow-Deutsher et al. 2010; Roth et al. 2011; Zhang et al. 2010), and there is evidence that these epigenetic modifications can be passed to offspring (e.g., Franklin et al. 2010). Human studies suggest that childhood trauma exposure is associated with methylation in specific genes, including the promoter region of the serotonin transporter (Beach et al. 2010, 2011; Smith et al. 2011) and the glucocorticoid receptor (McGowan et al. 2009). Microarray methylation studies have identified differences in methylation patterns for persons with and without PTSD and MDD (Fuchikami et al. 2011; Smith et al. 2011; Uddin et al. 2010, 2011). Finally, studies that integrate gene expression and methylation data have found evidence of different psychobiological pathways for PTSD among those with and without histories of childhood trauma (Mehta et al. 2013). A recent review of sex differences in DNA methylation associated with PTSD and depression suggests that neurodevelopmental changes in methylation may lay the groundwork for stress differences in reactions to stress that give rise to gender differences in the prevalence of stress-related disorders (Uddin et al. 2013). Specifically, in rodent models, sex-specific methylation at CpG sites in the estrogen receptor interacts with neonatal hormone exposure during sensitive periods to differentially effect brain development that could, in part, explain females' increased susceptibility to psychopathology in adulthood (Kurian et al. 2010; Schwarz et al. 2010).

Neural Circuitry

Trauma exposure also may influence the development of negative sequelae through structural or functional changes in the brain. A meta-analysis of brain imaging studies suggests that trauma exposure is associated with reduced volume in the hippocampus, a brain region implicated in episodic memory, relative to non-trauma exposed controls, and trauma victims with PTSD evidence even greater reductions in hippocampal volume compared to trauma victims without PTSD (Woon et al. 2010). Most brain imaging studies are cross-sectional, which limits conclusions about whether trauma exposure and PTSD decrease hippocampal volume or predispose persons to develop PTSD when exposed to a PTE. However, at least one study using monozygotic twins discordant for trauma exposure indicated that reduced

hippocampal volume is a preexisting risk factor for PTSD when exposed to PTEs, not an outcome of exposure to trauma (Gilbertson et al. 2002). Persons with PTSD and depression also show similar reductions in prefrontal cortex volume when compared to trauma-exposed healthy controls (Kroes et al. 2011). There is evidence of gender differences in brain development among children with and without child maltreatment histories and PTSD such that maltreated boys with PTSD evidence diminished volume in the corpus callosum and cerebrum and increased lateral ventricular volume relative to maltreated girls with PTSD and health controls (De Bellis and Keshavan 2003).

Neuroendocrine Pathways

Alterations in the hypothalamic-pituitary-adrenal (HPA) axis, the primary system involved in the physiological stress response (Sapolsky et al. 2000), have been observed among child abuse victims (e.g., Cicchetti et al. 2010; Shea et al. 2005; Trickett et al. 2010), sexual assault victims (e.g., Resnick et al. 1995; Yehuda and Bierer 2009), combat veterans (e.g., Boscarino, 1996), and motor vehicle accident survivors (Delahanty et al. 2000). In general, trauma victims evidence hypocortisolism, although one study found heightened daily cortisol among women with sexual abuse histories (Lemieux and Coe 1995). Blunted HPA axis responsivity also has been associated with the development and chronicity of PTSD among trauma victims (e.g., Bremner et al. 2003; Walsh et al. 2014; Yehuda et al. 1990). However, heightened cortisol responsivity has been observed among trauma victims with depression when exposed to psychosocial stressors (Burke et al. 2005). Thus, despite clear indications that trauma exposure is associated with HPA axis dysregulation, associations between common trauma-related sequelae like PTSD and depression and HPA axis functioning remain less clear. One study has suggested that prolonged childhood abuse, rather than the development of PTSD, MDD, or even BPD symptoms was associated with hyperresponsivity in the HPA axis (Rinne et al. 2002).

Psychological Factors

Trauma exposure may also influence the development of negative outcomes through cognitive and/or behavioral processes including shame, self-blame, cognitive distortions, and dysregulation in emotion regulation or coping. Developed to explain the negative sequelae of childhood sexual abuse, Finkelhor and Browne's (1985) traumagenic dynamics theory suggests that early life abuse can negatively shape a child's perception of his/herself, his/her behavior, and his/her interpersonal relationships, through four psychological processes that include traumatic sexualization, betrayal, shame/guilt, and powerlessness. These dynamics in turn have been associated with increased distress including PTSD, depression, and substance use disorders among victims of violence (Canton-Cortes et al. 2012; Walsh et al. 2014). Cognitive distortions including self-blame, hopelessness, and

preoccupation with danger also have been associated with more severe PTSD and with brain activation in regions that have previously been implicated in visual processing and autobiographic memory recall (Daniels et al. 2011). Cognitive distortions are also common among women dually diagnosed with PTSD and substance use disorders (Najavits et al. 2004).

Emotional dysregulation, which reflects difficulties identifying, modulating, and expressing emotions (Gratz and Roemer 2004; Gross 1998), is another domain of functioning that may be disrupted among victims of sexual violence. For example, families in which violence is occurring may provide few opportunities for children to observe and model emotion regulation abilities that allow for effective modulation of chronic negative affect. To cope, they may become emotionally or experientially avoidant, and when avoidance does not ameliorate distress, they may develop psychopathology (e.g., PTSD, MDD) and engage in external coping mechanisms including substance abuse and risky sexual behavior (Polusny and Follette 1995).

Support for emotion regulation and maladaptive coping or self-medication as explanatory mechanisms in the link between trauma exposure and negative sequelae stems from research documenting that emotion dysregulation underlies PTSD and MDD (e.g., Tull et al. 2007), and those with trauma histories report greater use of substances to reduce both negative affect (Grayson and Nolen-Hoeksema 2005) and PTSD symptoms (Miranda et al. 2002; Ullman et al. 2005). Hyperarousal symptoms, in particular, are associated with increased alcohol and drug use and dependence (e.g., Reed et al. 2007), and victims who report drinking to cope with distress or to reduce tension are more likely to develop problem drinking behaviors including alcohol abuse/dependence, blackouts, and increased tolerance (Ullman et al. 2005).

Diagnosis

Posttraumatic Stress Disorder

The most commonly assessed and diagnosed condition among trauma victims is posttraumatic stress disorder (PTSD). PTSD as defined in DSM-5 requires: (A) exposure to a PTE; (B) at least one of five possible reexperiencing symptoms (e.g., distressing thoughts/dreams, intense physiological/psychological responses to reminders of the trauma); (C) one of two possible avoidance symptoms (e.g., avoiding internal thoughts or feelings or external reminders of the trauma); (D) two of seven cognitive or mood-related symptoms (dissociative amnesia, persistent self-blame, persistent negative beliefs or emotions, constricted affect, anhedonia, or feelings of alienation); and (E) two of six arousal symptoms (e.g., sleep problems, irritability, heightened startle response, self-destructive behaviors, irritability/aggressiveness). Symptoms must be experienced with at least moderate frequency and severity in the previous month, and they must be associated with some degree of social or occupational functional impairment to yield a diagnosis.

Developmental Considerations

The DSM-5 also includes a developmental subtype of PTSD for children younger than 6 years old. Children younger than age 6 may lack the vocabulary and meta-awareness to describe their symptoms; therefore, DSM-5 criteria for preschool PTSD are more behaviorally grounded. With regard to reexperiencing symptoms, children do not always display overt distress when recollecting PTEs; therefore, no affect or excitement that accompanies a PTE recollection could qualify as a reexperiencing symptom. Only one symptom in the avoidance or negative alterations in cognitions and mood is necessary as these are the least frequent PTSD symptoms (Scheeringa et al. 2006). The wording of the symptoms "diminished interest in significant activities" and "feelings of detachment or estrangement" were changed to "constricted play" and "social withdrawal" for children under age 6. The arousal symptoms are already conducive to behavioral assessment; therefore, only the irritability symptom was changed to "extreme temper tantrums."

Depression

Frequently comorbid with PTSD (Nixon et al. 2004; Stein and Kennedy 2001), a diagnosis of depression requires depressed mood or anhedonia most days for the previous 2 weeks. It can also include significant changes in weight, appetite, or sleep, fatigue, guilt or feelings of worthlessness, problems with concentration, and suicidal ideation.

Other Anxiety Disorders

Approximately 70 % of trauma-exposed treatment-seeking patients report panic attack symptoms (Falsetti and Resnick 1997). Panic attack symptoms include heart palpitations, sweating, trembling/shaking, shortness of breath, a choking feeling, chest pain, nausea, feeling dizzy/lightheaded, derealization/depersonalization feelings, fear of losing control/going crazy, fear of dying, numbness/tingling, and chills/hot flashes. A panic attack is defined as experiencing four or more of these symptoms without warning or provocation; panic disorder refers to recurrent, unexpected panic attacks. Panic disorder cannot be diagnosed if the attacks only occur when exposed to a traumatic reminder.

Substance Use and Disorders

Trauma exposure has been associated with elevated risk for substance use disorders (Fetzner et al. 2011; Mills et al. 2006; Rees et al. 2011; Walsh et al. 2014); however, some research suggests that it is the development of PTSD, and not trauma exposure itself, that accounts for heighted risk for substance use and disorders (for review see

Breslau 2002). According to the self-medication model of substance use, trauma-exposed persons who develop PTSD, other anxiety symptoms, or depression may use substances to cope with these distressing symptoms (Khantzian 1997).

Evaluation

Clinical Interviews

Psychiatric conditions associated with PTE exposure have been assessed using various tools. The gold standard clinical interview for diagnosing PTSD is the Clinician Administered PTSD Scale (CAPS), which takes approximately 1 h to administer and includes a thorough evaluation of lifetime PTE exposure and the 17 PTSD items identified in the DSM-IV. Respondents are asked to separately rate the frequency and severity of each symptom in the preceding 2 weeks. The CAPS has been shown to have excellent reliability and validity, and consistent scores have been observed across items, raters, and testing occasions (Weathers et al. 2001). With regard to substance use, the Timeline Follow-back interview (Sobell and Sobell 1996) is a validated method to gather data on the patterns and frequency of substance use using a calendar method. The Structured Clinical Interview for DSM-IV also has been used extensively to diagnose PTSD, depression, other anxiety disorders, substance use disorders, and personality disorders.

Self-Report Measures

Although no substitute for diagnostic clinical interviews, a number of self-report measures with excellent reliability have been developed and validated against the gold standard clinical interviews. The PTSD Checklist (PCL; Weathers et al. 1999) has been developed in three formats – Civilian, Military, and Specific. Each version contains the 17 PTSD items from the DSM-IV and requires participants to rate their symptoms on a 0–4 severity scale. The Modified PTSD Symptom Scale-Self-Report (PSS-SR; Foa et al. 1993) is another 17-item measure of PTSD as assessed in the DSM-IV. Each symptom criterion is rated in terms of frequency of symptoms within the past 2 weeks on a scale of 0 = *not at all or only one time* to 3 = *almost always or five or more times per week*. Total scores range from 0 to 51. The PSS-SR has been shown to correlate highly with interview-based measures of PTSD (Foa et al. 1993) and has been used in numerous longitudinal studies assessing PTSD symptoms over time (e.g., Dunmore et al. 2001; Mayou et al. 2002). Measures such as the Davidson Trauma Scale, a self-report that separately assesses the frequency and severity of each DSM-IV symptom in the previous week on a scale from 0 to 4, also have been used to assess PTSD symptoms, particularly in SSRI trials (Davidson et al. 1997; 2002). Normative scores have been computed for comparison to the general population (Davidson et al. 2002).

Validated self-report measures for depression include the 21-item Beck Depression Inventory (BDI; Beck et al. 1988) and BDI-II (Dozois et al. 1998; Steer et al. 1997). The World Health Organization also has developed the Composite International Diagnostic Interview (CIDI; Wittchen 1994) that has been used in a number of epidemiologic studies (Kessler and Üstün 2004). Validated self-report measures for substance use and disorders include the Alcohol Use Disorders Identification Test (AUDIT; Saunders et al. 1993), a 10-item self-report measure of alcohol use and related problems, and the Drug Abuse Screening Test (DAST-10, Skinner 1982), a 10-item self-report measure of drug use and related problems.

Assessments for Children

The Child Behavior Checklist (CBCL; Achenbach et al. 2002) is a parent/teacher rated scale that measures broad aspects of internalizing and externalizing pathology including anxiety, depression, and anger; however, the CBCL does not capture aspects of functioning that may be particularly related to trauma exposure including intrusions, avoidance, and arousal. The Trauma symptom Checklist for Young Children is a 90-item caretaker completed checklist that assesses eight clinical scales including PTSD Intrusions (PTS-I), Avoidance (PTS-AV), Arousal (PTS-AR), and Total symptoms (PTS-TOT) as well as Sexual Concerns (SC), Dissociation (DIS), Anxiety (ANX), Depression (DEP), and Anger/Aggression (ANG) (Briere et al. 2001). The UCLA PTSD Index (Decker and Pynoos 2004) contains a thorough assessment of trauma exposure as well as the 17 items of PTSD in the DSM-IV. The Children's Depression Inventory (CDI) is a 27-item self-report scale appropriate for children age 7 to 17 that has good reliability and validity with normative scores to facilitate age comparisons (Kovacs 2004).

Pharmacotherapy

Numerous medications have been shown to effectively treat PTSD including tricyclic antidepressants, monoamine oxidase inhibitors, and serotonin reuptake inhibitors (SSRIs); however, SSRIs show the greatest efficacy with the fewest side effects (Albucher and Liberzon 2002). SSRIs such as sertraline, paroxetine, and fluoxetine are commonly prescribed to treat the symptoms of PTSD (Asnis et al. 2004), with sertraline and paroxetine producing reductions in PTSD symptoms in randomized controlled trials (Brady et al. 2000), and receiving FDA approval for the treatment of PTSD in adults. Some sex differences have been found with regard to treatment response to SSRIs. Specifically, women show a more positive treatment response to SSRIs compared to men (Khan et al. 2005; Young et al. 2009). For example, in depressed outpatients, women had a more positive response to the SSRI sertraline compared to the tricyclic imipramine, and men showed a stronger response to imipramine compared to sertraline (Kornstein et al. 2000). Sex hormones appeared to

play a role in treatment response as premenopausal women responded better to sertraline compared to imipramine, while postmenopausal women responded equally well to both medications (Kornstein et al. 2000). To date, no medications have been approved for use in children (Drury and Henry 2012). In PTSD patients with limited responsivity to SSRI treatment, augmentation with an atypical antipsychotic, Olanzipine, has been shown to produce better outcomes (Stein et al. 2002b). While psychopharmacologic interventions can be part of effective treatment for PTSD, findings are limited by high dropout rates in clinical trials, and negative side effects of these medications may explain poor retention in clinical trials (Albucher and Liberzon 2002).

Psychotherapy

A number of exposure-based treatments have been shown to be effective for the treatment of PTSD. For example, Prolonged Exposure (PE), which requires participants to use imaginal exercises to expose themselves to the memory of their PTE and the physical sensations and thoughts that arose during the PTE (Foa et al. 2007), has evidenced large effect sizes for the treatment of PTSD (Powers et al. 2010). PE was originally designed to treat PTSD associated with sexual violence (Foa et al. 1991), but has successfully been extended to other populations including combat veterans and adolescents (Gilboa-Schechtman et al. 2010).

Cognitive Processing Therapy (CPT), which exposes patients to the thoughts and emotions associated with their PTE through a combination of writing and thought challenging exercises, also has been shown to be effective in reducing PTSD symptoms (Resick et al. 2002). However, CPT contains modules that specifically address guilt, shame, and interpersonal difficulties, and thus yields greater reductions in guilt when compared to PE (Resick et al. 2002). Furthermore, dismantling studies have shown that the cognitive component alone has a stronger effect on reducing symptoms compared to the writing component alone (Resick et al. 2008).

Eye Movement Desensitization and Reprocessing (EMDR), which involves imaginal exposure while receiving bilateral sensory input that encourages eye movements, is another form of exposure treatment that shows similar reductions to those found with PE and greater reductions in symptoms relative to a wait-list control (Rothbaum et al. 2005). Meta-analyses support these findings by showing that EMDR is equally efficacious relative to trauma-focused cognitive behavioral therapy such as PE and CPT (Seidler and Wagner 2006).

Stress Inoculation Training (SIT), which involves psychoeducation and coping skills to increase resilience to stress (Meichenbaum 1974), has been applied to trauma victims (Veronen and Kilpatrick 1989). At posttreatment, SIT has been shown to be more effective at reducing PTSD symptoms than supportive counseling or a wait-list control (Foa et al. 1991); SIT and PE were associated with comparable posttreatment reductions in PTSD, although PE was associated with further reductions in PTSD at 3 months follow-up (Foa et al. 1991). In a follow-up study, PE was associated with greater posttreatment reductions in anxiety, social adjustment, and

PTSD severity when compared to SIT, SIT plus PE (SITP), or a wait-list control (Foa et al. 1999). In a separate investigation comparing EMDR to SITPE, EMDR was associated with greater reductions in reexperiencing symptoms relative to SITPE (Lee et al. 2002).

Psychotherapies for Children

Trauma-focused cognitive behavioral therapy is a developmentally appropriate evidence-based treatment for trauma symptoms among trauma-exposed children (Cohen et al. 2004; Deblinger et al. 2006, 2011). TF-CBT involves the child and non-offending caregiver and includes psychoeducation, coping skills, and in vivo exposure through the construction of a trauma narrative that can be completed in a developmentally appropriate manner. TF-CBT has been shown to improve trauma symptoms, parenting skills, and child personal safety skills (Deblinger et al. 2011).

Treatments for Comorbid Conditions

As noted previously, PTSD and SUDs are frequently comorbid. However, conventional wisdom has often suggested that treating PTSD using difficult exposure techniques in a person with an active SUD may exacerbate the SUD. Consequently, many PTSD treatment programs require patients to receive SUD treatment prior to beginning PTSD treatment. However, patients are often disconnected from services when transitioning from one provider to another, suggesting that evidence-based treatments targeting multiple conditions are much needed. During the past decade, several studies have begun to highlight promising results for the simultaneous treatment of comorbid conditions. For instance, cognitive behavioral treatment for women with PTSD and SUD has been shown to reduce PTSD and SUD symptoms at 3 months follow-up compared to women in a wait-list control group (Cohen and Hien 2006). PE for women with comorbid PTSD and SUD has been shown to reduce PTSD symptoms without increasing SUD symptoms (Mills et al. 2012). CPT also is effective at reducing PTSD symptoms among veterans with comorbid PTSD and AUD (Kaysen et al. 2013). Women with comorbid PTSD and SUD who were randomized to trauma-focused therapy versus a health education program evidenced greater reductions in PTSD symptoms and those who maintained these reductions were more likely show substance use improvement (Hien et al. 2010). Imaginal and in vivo exposure therapy for PTSD plus cognitive behavioral treatment for cocaine dependence was associated with significant pre-post reductions PTSD symptoms and cocaine use (Brady et al. 2001); however, a high degree of dropout was noted. Finally, a recent study examining combined PE and naltrexone for the treatment of comorbid PTSD and AUD found that the combined approach was associated with greater reductions in drinking days relative to either of the individual approaches (Foa et al. 2013).

PTSD is also highly comorbid with mood and other anxiety disorders and symptoms including depression and panic attacks. Given its focus on changing cognitive distortions that may be shared by both PTSD and MDD, CPT has been shown to result in concurrent changes in PTSD and depression symptoms (Liverant et al. 2012). Multiple channel exposure therapy, an evidence-based treatment that includes exposure to panic symptoms as well as imaginal exposure to the PTE, has been shown to effectively reduce comorbid PTSD and panic attacks (Falsetti et al. 2005, 2008). Other comorbid problems like affect dysregulation or interpersonal difficulties that are frequently present among trauma-exposed persons with PTSD may be targeted through treatments like Skills Training in Affective and Interpersonal Regulation (STAIR) followed by exposure therapy. Adult women with child sexual abuse histories who participate in STAIR evidence reductions in PTSD symptoms as well as affect dysregulation and interpersonal problems compared to wait-list controls (Cloitre et al. 2002).

Conclusions

Trauma exposure is prevalent and associated with a wide range of mental health and substance use disorders. Although men are slightly more likely to be exposed to any PTE, women are twice as likely to develop PTSD when exposed. The etiology of gender differences in posttraumatic sequelae may have yet to be elucidated, but may include genetic, neural circuitry, and psychological phenomena. Valid and reliable interviews and self-report measures are available for the assessment of trauma-related conditions. Changes have been made to the criteria for PTSD in DSM-5. Comorbidity is the rule rather than the exception among trauma-exposed persons; however, only in the last decade have treatment outcome studies shown that multiple co-occurring outcomes can be targeted simultaneously. Whether there are gender differences in treatment, response or treatment matching deserves further examination. Despite a large body of work on gender, trauma exposure, and trauma-related disorders, more research is needed to identify the mechanisms by which gender shapes response to PTEs and treatment for posttraumatic sequelae.

References

Achenbach TM, Dumenci L, Rescorla LA (2002) Ten-year comparisons of problems and competencies for national samples of youth self, parent, and teacher reports. J Emot Behav Disord 10(4):194–203

Albucher RC, Liberzon I (2002) Psychopharmacological treatment in PTSD: a critical review. J Psychiatr Res 36(6):355–367

Asnis GM, Kohn SR, Henderson M, Brown NL (2004) SSRIs versus non-SSRIs in post-traumatic stress disorder. Drugs 64(4):383–404

Bailey JN, Goenjian AK, Noble EP, Walling DP, Ritchie T, Goenjian HA (2010) PTSD and dopaminergic genes, DRD2 and DAT, in multigenerational families exposed to the Spitak earthquake. Psychiatry Res 178(3):507–510

Beach SR, Brody GH, Todorov AA, Gunter TD, Philibert RA (2010) Methylation at SLC6A4 is linked to family history of child abuse: an examination of the Iowa Adoptee sample. American Journal of Medical Genetics Part B: Neuropsychiatric Genetics 153(2):710–713

Beach SR, Brody GH, Todorov AA, Gunter TD, Philibert RA (2011) Methylation at 5HTT mediates the impact of child sex abuse on women's antisocial behavior: an examination of the Iowa adoptee sample. Psychosomatic medicine 73(1):83

Beck AT, Steer RA, Carbin MG (1988) Psychometric properties of the beck depression inventory: twenty-five years of evaluation. Clin Psychol Rev 8(1):77–100

Binder EB, Bradley RG, Liu W, Epstein MP, Deveau TC, Mercer KB, Ressler KJ (2008) Association of FKBP5 polymorphisms and childhood abuse with risk of posttraumatic stress disorder symptoms in adults. Jama 299(11):1291–1305

Black MC, Basile KC, Breiding MJ, Smith SG, Walters ML, Merrick MT, Chen J, Stevens MR (2011) National intimate partner and sexual violence survey. Centers for Disease Control and Prevention, Atlanta

Blanco C, Xu Y, Brady K, Pérez-Fuentes G, Okuda M, Wang S (2013) Comorbidity of posttraumatic stress disorder with alcohol dependence among US adults: results from National Epidemiological Survey on Alcohol and Related Conditions. Drug Alcohol Depend 132(3): 630–638

Bohnert KM, Breslau N (2011) Assessing the performance of the short screening scale for posttraumatic stress disorder in a large nationally-representative survey. Int J Methods Psychiatr Res 20(1):e1–e5

Bonanno GA (2005) Resilience in the face of potential trauma. Curr Dir Psychol Sci 14(3):135–138

Boscarino JA (1996) Posttraumatic stress disorder, exposure to combat, and lower plasma cortisol among Vietnam veterans: findings and clinical implications. Journal of Consulting and Clinical Psychology 64(1):191

Brady K, Pearlstein T, Asnis GM, Baker D, Rothbaum B, Sikes CR, Farfel GM (2000) Efficacy and safety of sertraline treatment of posttraumatic stress disorder: a randomized controlled trial. JAMA 283(14):1837–1844

Brady KT, Dansky BS, Back SE, Foa EB, Carroll KM (2001) Exposure therapy in the treatment of PTSD among cocaine-dependent individuals: preliminary findings. J Subst Abuse Treat 21(1):47–54

Bremner JD, Vythilingam M, Vermetten E, Adil J, Khan S, Nazeer A, Afzal N, McGlashan T, Elzinga B, Anderson GM, Heninger G, Southwick SM, Charney DS (2003) Cortisol response to a cognitive stress challenge in posttraumatic stress disorder (PTSD) related to childhood abuse. Psychoneuroendocrinology 28(6):733–750

Breslau N (2002) In review. Can J Psychiatry 47:923–929

Breslau N (2009) The epidemiology of trauma, PTSD, and other posttrauma disorders. Trauma Violence Abuse 10(3):198–210

Breslau N, Anthony JC (2007) Gender differences in the sensitivity to posttraumatic stress disorder: an epidemiological study of urban young adults. J Abnorm Psychol 116(3):607

Breslau N, Davis GC (1992) Posttraumatic stress disorder in an urban population of young adults: risk factors for chronicity. Am J Psychiatry 149:671–675

Breslau N, Davis GC, Peterson EL, Schultz L (1997) Psychiatric sequelae of posttraumatic stress disorder in women. Arch Gen Psychiatry 54(1):583–584

Briere J, Johnson K, Bissada A, Damon L, Crouch J, Gil E, Ernst V (2001) The trauma symptom checklist for young children (TSCYC): reliability and association with abuse exposure in a multi-site study. Child Abuse Negl 25(8):1001–1014

Burke HM, Davis MC, Otte C, Mohr DC (2005) Depression and cortisol responses to psychological stress: a meta-analysis. Psychoneuroendocrinology 30(9):846–856

Campbell J, Garcia-Moreno C, Sharps P (2004) Abuse during pregnancy in industrialized and developing countries. Violence Against Women 10(7):770–789

Canton-Cortes D, Cortés MR, Canton J (2012) The role of traumagenic dynamics on the psychological adjustment of survivors of child sexual abuse. Eur J Dev Psychol 9(6):665–680

Chang SC, Xie P, Anton RF, De Vivo I, Farrer LA, Kranzler HR, Oslin D, Purcell SM, Roberts AL, Smoller JW, Uddin M, Gelernter J, Koenen KC (2011) No association between ADCYAP1R1 and post-traumatic stress disorder in two independent samples. Mol Psychiatry 17(3): 239–241

Chertkow-Deutsher Y, Cohen H, Klein E, Ben-Shachar D (2010) DNA methylation in vulnerability to post-traumatic stress in rats: evidence for the role of the post-synaptic density protein Dlgap2. Int J Neuropsychopharmacol 13(03):347–359
Cicchetti D, Rogosch FA, Gunnar MR, Toth SL (2010) The differential impacts of early physical and sexual abuse and internalizing problems on daytime cortisol rhythm in school-aged children. Child Dev 81(1):252–269
Cloitre M, Koenen KC, Cohen LR, Han H (2002) Skills training in affective and interpersonal regulation followed by exposure: a phase-based treatment for PTSD related to childhood abuse. J Consult Clin Psychol 70(5):1067
Cohen LR, Hien DA (2006) Treatment outcomes for women with substance abuse and PTSD who have experienced complex trauma. Psychiatr Serv 57(1):100–106
Cohen JA, Deblinger E, Mannarino AP (2004) Trauma focused cognitive behavioral therapy for sexually abused children. Psychiatr Times 21(10):109–121
Cornelis MC, Nugent NR, Amstadter AB, Koenen KC (2010) Genetics of post-traumatic stress disorder: review and recommendations for genome-wide association studies. Curr Psychiatry Rep 12(4):313–326
Cortina LM, Kubiak SP (2006) Gender and posttraumatic stress: sexual violence as an explanation for women's increased risk. J Abnorm Psychol 115(4):753
Cuijpers P, Smit F (2002) Excess mortality in depression: a meta-analysis of community studies. J Affect Disord 72(3):227–236
Cuijpers P, Vogelzangs N, Twisk J, Kleiboer A, Li J, Penninx BW (2013) Differential mortality rates in major and subthreshold depression: meta-analysis of studies that measured both. Br J Psychiatry 202(1):22–27
Daniels JK, Hegadoren K, Coupland NJ, Rowe BH, Neufeld RW, Lanius RA (2011) Cognitive distortions in an acutely traumatized sample: an investigation of predictive power and neural correlates. Psychol Med 41(10):2149–2157
Davidson JR, Book SW, Colket JT, Tupler LA, Roth S, David D, Feldman ME (1997) Assessment of a new self-rating scale for post-traumatic stress disorder. Psychol Med 27(1):153–160
Davidson JR, Tharwani HM, Connor KM (2002) Davidson trauma scale (DTS): normative scores in the general population and effect sizes in placebo-controlled SSRI trials. Depress Anxiety 15(2):75–78
De Bellis MD, Keshavan MS (2003) Sex differences in brain maturation in maltreatment-related pediatric posttraumatic stress disorder. Neurosci Biobehav Rev 27(1):103–117
Deblinger E, Mannarino AP, Cohen JA, Steer RA (2006) A follow-up study of a multisite, randomized, controlled trial for children with sexual abuse-related PTSD symptoms. J Am Acad Child Adolesc Psychiatry 45(12):1474–1484
Deblinger E, Mannarino AP, Cohen JA, Runyon MK, Steer RA (2011) Trauma-focused cognitive behavioral therapy for children: impact of the trauma narrative and treatment length. Depress Anxiety 28(1):67–75
Decker KB, Pynoos RS (2004) The University of California at Los Angeles post-traumatic stress disorder reaction index. Curr Psychiatry Rep 6(2):96–100
Delahanty DL, Raimonde AJ, Spoonster E (2000) Initial posttraumatic urinary cortisol levels predict subsequent PTSD symptoms in motor vehicle accident victims. Biol Psychiatry 48(9):940–947
Dick DM, Foroud T (2003) Candidate genes for alcohol dependence: a review of genetic evidence from human studies. Alcoholism: Clinical and Experimental Research 27(5):868–879
Dozois DJ, Dobson KS, Ahnberg JL (1998) A psychometric evaluation of the Beck Depression Inventory–II. Psychol Assess 10(2):83
Drury SS, Henry C (2012) Evidenced-based treatment of PTSD in children and adolescents: where does psychopharmacology fit? Child Adolesc Psychopharmacol News 17(3):1–8
Drury SS, Theall KP, Keats BJ, Scheeringa M (2009) The role of the dopamine transporter (DAT) in the development of PTSD in preschool children. J Trauma Stress 22(6):534–539
Dunmore E, Clark DM, Ehlers A (2001) A prospective investigation of the role of cognitive factors in persistent posttraumatic stress disorder (PTSD) after physical or sexual assault. Behav Res Ther 39(9):1063–1084

Falsetti SA, Resnick HS, Davis J (2005) Multiple channel exposure therapy combining cognitive-behavioral therapies for the treatment of posttraumatic stress disorder with panic attacks. Behav Modif 29(1):70–94

Falsetti SA, Resnick HS, Davis JL (2008) Multiple channel exposure therapy for women with PTSD and comorbid panic attacks. Cogn Behav Ther 37(2):117–130

Fetzner MG, McMillan KA, Sareen J, Asmundson GJ (2011) What is the association between traumatic life events and alcohol abuse/dependence in people with and without PTSD? Findings from a nationally representative sample. Depress Anxiety 28(8):632–638

Finkelhor D (1994) The international epidemiology of child sexual abuse. Child Abuse Negl 18(5):409–417

Finkelhor D, Browne A (1985) The traumatic impact of child sexual abuse: a conceptualization. Am J Orthopsychiatry 55(4):530

Finkelhor D, Jones L (2006) Why have child maltreatment and child victimization declined? J Soc Issues 62(4):685–716

Foa EB, Rothbaum BO, Riggs DS, Murdock TB (1991) Treatment of posttraumatic stress disorder in rape victims: a comparison between cognitive-behavioral procedures and counseling. J Consult Clin Psychol 59(5):715

Foa EB, Riggs DS, Dancu CV, Rothbaum BO (1993) Reliability and validity of a brief instrument for assessing post-traumatic stress disorder. J Trauma Stress 6(4):459–473

Foa EB, Dancu CV, Hembree EA, Jaycox LH, Meadows EA, Street GP (1999) A comparison of exposure therapy, stress inoculation training, and their combination for reducing posttraumatic stress disorder in female assault victims. J Consult Clin Psychol 67(2):194

Foa E, Hembree E, Rothbaum BO (2007) Prolonged exposure therapy for PTSD: emotional processing of traumatic experiences therapist guide. Oxford University Press, Oxford, UK

Foa EB, Yusko DA, McLean CP, Suvak MK, Bux DA, Oslin D, Volpicelli J (2013) Concurrent naltrexone and prolonged exposure therapy for patients with comorbid alcohol dependence and PTSD: a randomized clinical trial. JAMA 310(5):488–495

Franklin TB, Russig H, Weiss IC, Gräff J, Linder N, Michalon A, Vizi S, Mansuy IM (2010) Epigenetic transmission of the impact of early stress across generations. Biol Psychiatry 68(5):408–415

Fuchikami M, Morinobu S, Segawa M, Okamoto Y, Yamawaki S, Ozaki N, Inoue T, Kusumi I, Koyama T, Tsuchiyama K, Terao T (2011) DNA methylation profiles of the brain-derived neurotrophic factor (BDNF) gene as a potent diagnostic biomarker in major depression. PLoS One 6(8):e23881

World Health Organization (2013) Global and regional estimates of violence against women: prevalence and health effects of intimate partner violence and non-partner sexual violence. World Health Organization

Gelernter J, Kranzler HR, Sherva R, Almasy L, Koesterer R, Smith AH, Farrer LA (2014) Genome-wide association study of alcohol dependence: significant findings in African-and European-Americans including novel risk loci. Mol Psychiatry 19:41–49

Gilbertson MW, Shenton ME, Ciszewski A, Kasai K, Lasko NB, Orr SP, Pitman RK (2002) Smaller hippocampal volume predicts pathologic vulnerability to psychological trauma. Nat Neurosci 5(11):1242–1247

Gilboa-Schechtman E, Foa EB, Shafran N, Aderka IM, Powers MB, Rachamim L, Apter A (2010) Prolonged exposure versus dynamic therapy for adolescent PTSD: a pilot randomized controlled trial. J Am Acad Child Adolesc Psychiatry 49(10):1034–1042

Grabe HJ, Schwahn C, Mahler J, Appel K, Schulz A, Spitzer C, Fenske K, Barnow S, Freyberger HJ, Teumer A, Petersmann A, Biffar R, Rosskopf D, John U, Völzke H (2012) Genetic epistasis between the brain-derived neurotrophic factor Val66Met polymorphism and the 5-HTT promoter polymorphism moderates the susceptibility to depressive disorders after childhood abuse. Prog NeuroPsychopharmacol Biol Psychiatry 36(2):264–270

Gratz KL, Roemer L (2004) Multidimensional assessment of emotion regulation and dysregulation: development, factor structure, and initial validation of the difficulties in emotion regulation scale. J Psychopathol Behav Assess 26(1):41–54

Grayson CE, Nolen-Hoeksema S (2005) Motives to drink as mediators between childhood sexual assault and alcohol problems in adult women. J Trauma Stress 18(2):137–145
Gross JJ (1998) The emerging field of emotion regulation: an integrative review. Rev Gen Psychol 2(3):271
Guffanti G, Galea S, Yan L, Roberts AL, Solovieff N, Aiello AE, Koenen KC (2013) Genome-wide association study implicates a novel RNA gene, the lincRNA, AC068718, as a risk factor for post-traumatic stress disorder in women. Psychoneuroendocrinology 38(12):3029–3038
Haastrup E, Bukh JD, Bock C, Vinberg M, Thørner LW, Hansen T, Werge T, Kessing LV, Ullum H (2012) Promoter variants in *IL18* are associated with onset of depression in patients previously exposed to stressful-life events. J Affect Disord 136(1):134–138
Heise LL, Raikes A, Watts CH, Zwi AB (1994) Violence against women: a neglected public health issue in less developed countries. Soc Sci Med 39(9):1165–1179
Hien DA, Jiang H, Campbell AN, Hu MC, Miele GM, Cohen LR, Nunes EV (2010) Do treatment improvements in PTSD severity affect substance use outcomes? A secondary analysis from a randomized clinical trial in NIDA's Clinical Trials Network. Am J Psychiatry 167(1):95
Kaysen D, Lindgren K, Zangana GAS, Murray L, Bass J, Bolton P (2013) Adaptation of cognitive processing therapy for treatment of torture victims: experience in Kurdistan, Iraq. Psychol Trauma: Theory Res Pract Policy 5(2):184
Kendler KS, Gatz M, Gardner CO, Pedersen NL (2006) A Swedish national twin study of lifetime major depression. Am J Psychiatry 163(1):109–114
Kessler RC (2000) Posttraumatic stress disorder: the burden to the individual and to society. J Clin Psychiatry 61:4–12
Kessler RC, Üstün TB (2004) The world mental health (WMH) survey initiative version of the world health organization (WHO) composite international diagnostic interview (CIDI). Int J Methods Psychiatr Res 13(2):93–121
Kessler RC, Sonnega A, Bromet E, Hughes M, Nelson CB (1995) Posttraumatic stress disorder in the National Comorbidity Survey. Arch Gen Psychiatry 52(12):1048
Khan A, Brodhead AE, Schwartz KA, Kolts RL, Brown WA (2005) Sex differences in antidepressant response in recent antidepressant clinical trials. J Clin Psychopharmacol 25(4):318–324
Khantzian EJ (1997) The self-medication hypothesis of substance use disorders: a reconsideration and recent applications. Harv Rev Psychiatry 4(5):231–244
Kilpatrick DG, Edmunds CN, Seymour AK (1992) Rape in America: a report to the nation. National Victim Center & The Crime Victims Center, Charleston
Koenen KC, Fu QJ, Ertel K, Lyons MJ, Eisen SA, True WR, Goldberg J, Tsuang MT (2008a) Common genetic liability to major depression and posttraumatic stress disorder in men. J Affect Disord 105(1):109–115
Koenen KC, Nugent NR, Amstadter AB (2008b) Gene-environment interaction in posttraumatic stress disorder. Eur Arch Psychiatry Clin Neurosci 258(2):82–96
Koenen KC, Amstadter AB, Nugent NR (2009) Gene-environment interaction in posttraumatic stress disorder: an update. J Trauma Stress 22(5):416–426
Kornstein SG, Schatzberg AF, Thase ME, Yonkers KA, McCullough JP, Keitner GI, Gelenberg AJ, Davis SM, Harrison WM, Keller MB (2000) Gender differences in treatment response to sertraline versus imipramine in chronic depression. Am J Psychiatry 157(9):1445–1452
Kovacs M (2004) Children's depression inventory (CDI). Multi-Health Systems, Toronto
Kroes MC, Rugg MD, Whalley MG, Brewin CR (2011) Structural brain abnormalities common to posttraumatic stress disorder and depression. J Psychiatry Neurosci 36(4):256
Kurian JR, Olesen KM, Auger AP (2010) Sex differences in epigenetic regulation of the estrogen receptor-α promoter within the developing preoptic area. Endocrinology 151(5):2297–2305
Lee C, Gavriel H, Drummond P, Richards J, Greenwald R (2002) Treatment of PTSD: stress inoculation training with prolonged exposure compared to EMDR. J Clin Psychol 58(9):1071–1089
Lemieux AM, Coe CL (1995) Abuse-related posttraumatic stress disorder: evidence for chronic neuroendocrine activation in women. Psychosom Med 57(2):105–115
Liverant GI, Suvak MK, Pineles SL, Resick PA (2012) Changes in posttraumatic stress disorder and depressive symptoms during cognitive processing therapy: evidence for concurrent change. J Consult Clin Psychol 80(6):957

Logue MW, Baldwin C, Guffanti G, Melista E, Wolf EJ, Reardon AF, Uddin M, Wildman D, Galea S, Koenen KC, Miller MW (2013) A genome-wide association study of post-traumatic stress disorder identifies the retinoid-related orphan receptor alpha (RORA) gene as a significant risk locus. Mol Psychiatry 18:937–942

Lyons MJ, Goldberg J, Eisen SA, True W, Tsuang MT, Meyer JM, Henderson WG (1993) Do genes influence exposure to trauma? A twin study of combat. Am J Med Genet 48(1):22–27

Lyons MJ, Eisen SA, Goldberg J, True W, Lin N, Meyer JM, Toomey R, Faraone SV, Merla-Ramos M, Tsuang MT (1998) A registry-based twin study of depression in men. Arch Gen Psychiatry 55(5):468–472

Mayou RA, Ehlers A, Bryant B (2002) Posttraumatic stress disorder after motor vehicle accidents: 3-year follow-up of a prospective longitudinal study. Behav Res Ther 40(6):665–675

McGowan PO, Sasaki A, D'Alessio AC, Dymov S, Labonté B, Szyf M, Meaney MJ (2009) Epigenetic regulation of the glucocorticoid receptor in human brain associates with childhood abuse. Nat Neurosci 12(3):342–348

McLeod DS, Koenen KC, Meyer JM, Lyons MJ, Eisen S, True W, Goldberg J (2001) Genetic and environmental influences on the relationship among combat exposure, posttraumatic stress disorder symptoms, and alcohol use. J Trauma Stress 14:259–275

Mehta D, Binder EB (2012) Gene× environment vulnerability factors for PTSD: The HPA-axis. Neuropharmacology 62(2);654–662

Mehta D, Klengel T, Conneely KN, Smith AK, Altmann A, Pace TW, Binder EB (2013) Childhood maltreatment is associated with distinct genomic and epigenetic profiles in posttraumatic stress disorder. Proc Natl Acad Sci 110(20):8302–8307

Meichenbaum D (1974) Cognitive behavior modification. General Learning Press, Morristown

Mills K, Teesson M, Ross J, Peters L (2006) Trauma, PTSD, and substance use disorders: findings from the Australian National Survey of Mental Health and Well-Being. Am J Psychiatry 163(4):652–658

Mills KL, Teesson M, Back SE, Brady KT, Baker AL, Hopwood S, Sannibale C, Barrett EL, Merz S, Rosenfeld J, Ewer PL (2012) Integrated exposure-based therapy for co-occurring posttraumatic stress disorder and substance dependence: a randomized controlled trial. JAMA 308(7):690–699

Miranda R, Meyerson LA, Long PJ, Marx BP, Simpson SM (2002) Sexual assault and alcohol use: exploring the self-medication hypothesis. Violence Vict 17(2):205–217

Najavits LM, Gotthardt S, Weiss RD, Epstein M (2004) Cognitive distortions in the dual diagnosis of PTSD and substance use disorder. Cogn Ther Res 28(2):159–172

Nixon RD, Resick PA, Nishith P (2004) An exploration of comorbid depression among female victims of intimate partner violence with posttraumatic stress disorder. J Affect Disord 82(2):315–320

Norris FH, Tracy M, Galea S (2009) Looking for resilience: understanding the longitudinal trajectories of responses to stress. Soc Sci Med 68(12):2190–2198

Nugent NR, Amstadter AB, Koenen KC (2008) Genetics of post-traumatic stress disorder: informing clinical conceptualizations and promoting future research. Am J Med Genet C: Sem Med Genet 148(2):127–132

Pereda N, Guilera G, Forns M, Gómez-Benito J (2009) The prevalence of child sexual abuse in community and student samples: a meta-analysis. Clin Psychol Rev 29(4):328–338

Perkonigg A, Kessler RC, Storz S, Wittchen HU (2000) Traumatic events and post-traumatic stress disorder in the community: prevalence, risk factors and comorbidity. Acta Psychiatr Scand 101(1):46–59

Perry BL, Pescosolido BA, Bucholz K, Edenberg H, Kramer J, Kuperman S, Schuckit MA, Nurnberger JI Jr (2013) Gender-specific gene–environment interaction in alcohol dependence: the impact of daily life events and GABRA2. Behav Genet 43(5):402–414

Pietrzak RH, Goldstein RB, Southwick SM, Grant BF (2011) Prevalence and Axis I comorbidity of full and partial posttraumatic stress disorder in the United States: results from Wave 2 of the National Epidemiologic Survey on Alcohol and Related Conditions. J Anxiety Disord 25(3):456–465

Polusny MA, Follette VM (1995) Long-term correlates of child sexual abuse: theory and review of the empirical literature. Appl Prev Psychol 4(3):143–166

Powers MB, Halpern JM, Ferenschak MP, Gillihan SJ, Foa EB (2010) A meta-analytic review of prolonged exposure for posttraumatic stress disorder. Clin Psychol Rev 30(6):635–641

Qureshi SU, Pyne JM, Magruder KM, Schulz PE, Kunik ME (2009) The link between post-traumatic stress disorder and physical comorbidities: a systematic review. Psychiatric quarterly, 80(2), 87–97

Reed PL, Anthony JC, Breslau N (2007) Incidence of drug problems in young adults exposed to trauma and posttraumatic stress disorder: do early life experiences and predispositions matter? Arch Gen Psychiatry 64(12):1435–1442

Rees S, Silove D, Chey T, Ivancic L, Steel Z, Creamer M, Forbes D (2011) Lifetime prevalence of gender-based violence in women and the relationship with mental disorders and psychosocial function. JAMA 306(5):513–521

Rehm J, Mathers C, Popova S, Thavorncharoensap M, Teerawattananon Y, Patra J (2009) Global burden of disease and injury and economic cost attributable to alcohol use and alcohol-use disorders. Lancet 373(9682):2223–2233

Resick PA, Nishith P, Weaver TL, Astin MC, Feuer CA (2002) A comparison of cognitive-processing therapy with prolonged exposure and a waiting condition for the treatment of chronic posttraumatic stress disorder in female rape victims. J Consult Clin Psychol 70(4):867

Resick PA, Galovski TE, Uhlmansiek MOB, Scher CD, Clum GA, Young-Xu Y (2008) A randomized clinical trial to dismantle components of cognitive processing therapy for posttraumatic stress disorder in female victims of interpersonal violence. J Consult Clin Psychol 76(2):243

Resnick HS, Kilpatrick DG, Dansky BS, Saunders BE, Best CL (1993) Prevalence of civilian trauma and posttraumatic stress disorder in a representative national sample of women. J Consult Clin Psychol 61(6):984

Resnick HS, Yehuda R, Pitman RK, Foy DW (1995) Effect of previous trauma on acute plasma cortisol level following rape. Am J Psychiatry 152(11):1675–1677

Ressler KJ, Mercer KB, Bradley B, Jovanovic T, Mahan A, Kerley K, May V (2011) Post-traumatic stress disorder is associated with PACAP and the PAC1 receptor. Nature 470(7335):492–497

Rinne T, De Kloet ER, Wouters L, Goekoop JG, DeRijk RH, van den Brink W (2002) Hyperresponsiveness of hypothalamic-pituitary-adrenal axis to combined dexamethasone/corticotropin-releasing hormone challenge in female borderline personality disorder subjects with a history of sustained childhood abuse. Biol Psychiatry 52(11):1102–1112

Roberts AL, Gilman SE, Breslau J, Breslau N, Koenen KC (2011) Race/ethnic differences in exposure to traumatic events, development of post-traumatic stress disorder, and treatment-seeking for post-traumatic stress disorder in the United States. Psychol Med 41(1):71–83

Rodriguez P, Holowka DW, Marx BP (2012). Assessment of posttraumatic stress disorder-related functional impairment: a review. J Rehabil Res Dev 49(5):649–666

Roth TL, Zoladz PR, Sweatt JD, Diamond DM (2011) Epigenetic modification of hippocampal Bdnf DNA in adult rats in an animal model of post-traumatic stress disorder. J Psychiatr Res 45(7):919–926

Rothbaum BO, Astin MC, Marsteller F (2005) Prolonged exposure versus eye movement desensitization and reprocessing (EMDR) for PTSD rape victims. J Trauma Stress 18(6):607–616

Roy A, Gorodetsky E, Yuan Q, Goldman D, Enoch MA (2010) Interaction of FKBP5, a stress-related gene, with childhood trauma increases the risk for attempting suicide. Neuropsychopharmacology 35(8):1674–1683

Sapolsky RM, Romero LM, Munck AU (2000) How do glucocorticoids influence stress responses? Integrating permissive, suppressive, stimulatory, and preparative actions 1. Endocr Rev 21(1):55–89

Sarapas C, Cai G, Bierer LM, Golier JA, Galea S, Ising M, Yehuda R (2011) Genetic markers for PTSD risk and resilience among survivors of the World Trade Center attacks. Disease markers 30(2–3):101–110

Sartor CE, McCutcheon VV, Pommer NE, Nelson EC, Grant JD, Duncan AE, Heath AC (2011) Common genetic and environmental contributions to post-traumatic stress disorder and alcohol dependence in young women. Psychol Med 41(07):1497–1505

Sartor CE, Grant JD, Lynskey MT, McCutcheon VV, Waldron M, Statham DJ, Bucholz KK, Madden PA, Heath AC, Martin NG, Nelson EC (2012) Common heritable contributions to low-risk trauma, high-risk trauma, posttraumatic stress disorder, and major depression. Arch Gen Psychiatry 69(3):293

Saunders JB, Aasland OG, Babor TF, Grant M (1993) Development of the alcohol use disorders identification test (AUDIT): WHO collaborative project on early detection of persons with harmful alcohol consumption-II. Addiction 88(6):791–804

Scheeringa M, Wright M, Hunt J, Zeanah C (2006) Factors affecting the diagnosis and prediction of PTSD symptomatology in children and adolescents. American Journal of Psychiatry 163(4):644–651

Schwarz JM, Nugent BM, McCarthy MM (2010) Developmental and hormone-induced epigenetic changes to estrogen and progesterone receptor genes in brain are dynamic across the life span. Endocrinology 151(10):4871–4881

Segman RH, Cooper-Kazaz R, Macciardi F, Golster T, Halfon Y, Dobroborski T, Shalev AY (2002) Association between the dopamine transporter gene and posttraumatic strees disorder. Mol Psychiatry 7(8):903–907

Seidler GH, Wagner FE (2006) Comparing the efficacy of EMDR and trauma-focused cognitive-behavioral therapy in the treatment of PTSD: a meta-analytic study. Psychol Med 36(11):1515–1522

Shea A, Walsh C, MacMillan H, Steiner M (2005) Child maltreatment and HPA axis dysregulation: relationship to major depressive disorder and post traumatic stress disorder in females. Psychoneuroendocrinology 30(2):162–178

Skelton K, Ressler KJ, Norrholm SD, Jovanovic T, Bradley-Davino B (2012) PTSD and gene variants: new pathways and new thinking. Neuropharmacology 62(2):628–637

Skinner HA (1982) The drug abuse screening test. Addict Behav 7(4):363–371

Smith AK, Conneely KN, Kilaru V, Mercer KB, Weiss TE, Bradley B, Tang Y, Gillespie CF, Cubells JF, Ressler KJ (2011) Differential immune system DNA methylation and cytokine regulation in post-traumatic stress disorder. Am J Med Genet B Neuropsychiatr Genet 156(6):700–708

Sobell LC, Sobell MB (1996) Timeline followback user's guide: a calendar method for assessing alcohol and drug use. Addiction Research Foundation, Toronto

Steel Z, Chey T, Silove D, Marnane C, Bryant RA, Van Ommeren M (2009) Association of torture and other potentially traumatic events with mental health outcomes among populations exposed to mass conflict and displacement: a systematic review and meta-analysis. JAMA 302(5):537–549

Steer RA, Ball R, Raneeri WF, Beck AT (1997) Further evidence for the construct validity of the Beck Depression Inventory-II with psychiatric outpatients. Psychol Rep 80(2):443–446

Stein MB, Kennedy C (2001) Major depressive and post-traumatic stress disorder comorbidity in female victims of intimate partner violence. J Affect Disord 66(2):133–138

Stein MB, Jang KL, Taylor S, Vernon PA, Livesley WJ (2002a) Genetic and environmental influences on trauma exposure and posttraumatic stress disorder symptoms: a twin study. Am J Psychiatry 159(10):1675–1681

Stein MB, Kline NA, Matloff JL (2002b) Adjunctive olanzapine for SSRI-resistant combat-related PTSD: a double-blind, placebo-controlled study. Am J Psychiatry 159(10):1777–1779

Tolin DF, Foa EB (2006) Sex differences in trauma and posttraumatic stress disorder: a quantitative review of 25 years of research. Psychol Bull 132(6):959

Trickett PK, Noll JG, Susman EJ, Shenk CE, Putnam FW (2010) Attenuation of cortisol across development for victims of sexual abuse. Dev Psychopathol 22(01):165–175

True WR, Rice J, Eisen SA, Heath AC, Goldberg J, Lyons MJ, Nowak J (1993) A twin study of genetic and environmental contributions to liability for posttraumatic stress symptoms. Arch Gen Psychiatry 50(4):257–264

Tsai SJ, Cheng CY, Yu YWY, Chen TJ, Hong CJ (2003) Association study of a brain-derived neurotrophic-factor genetic polymorphism and major depressive disorders, symptomatology, and antidepressant response. Am J Med Genet B Neuropsychiatr Genet 123(1): 19–22

Tull MT, Barrett HM, McMillan ES, Roemer L (2007) A preliminary investigation of the relationship between emotion regulation difficulties and posttraumatic stress symptoms. Behav Ther 38(3):303–313

Uddin M, Aiello AE, Wildman DE, Koenen KC, Pawelec G, de Los Santos R, Galea S (2010) Epigenetic and immune function profiles associated with posttraumatic stress disorder. Proceedings of the National Academy of Sciences 107(20):9470–9475

Uddin M, Koenen KC, Aiello AE, Wildman DE, de Los Santos R, Galea S (2011) Epigenetic and inflammatory marker profiles associated with depression in a community-based epidemiologic sample. Psychological medicine 41(05):997–1007

Uddin M, Chang SC, Zhang C, Ressler K, Mercer KB, Galea S, Koenen KC (2013) Adcyap1r1 genotype, posttraumatic stress disorder, and depression among women exposed to childhood maltreatment. Depress Anxiety 30(3):251–258

Ullman SE, Filipas HH, Townsend SM, Starzynski LL (2005) Trauma exposure, posttraumatic stress disorder and problem drinking in sexual assault survivors. J Stud Alcohol Drugs 66(5):610

van Spijker BA, van Straten A, Kerkhof AJ, Hoeymans N, Smit F (2011) Disability weights for suicidal thoughts and non-fatal suicide attempts. J Affect Disord 134(1):341–347

Veronen LJ, Kilpatrick DG (1989) Stress management for rape victims. In: Stress reduction and prevention. Springer, New York, NY, pp 341–374

Walsh K, Latzman NE, Latzman RD (2014) Pathway from child sexual and physical abuse to risky sex among emerging adults: the role of trauma-related intrusions and alcohol problems. J Adolesc Health 54:442–448

Walsh K, Keyes KM, Koenen KC, Hasin D (2015) Lifetime prevalence of gender-based violence in US women: associations with mood/anxiety and substance use disorders. J Psychiatr Res 62:7–13

Walsh K, Hasin DS, Keyes KM, Koenen KC (under revision). Associations between gender-based violence and personality disorders in US women. Personality Disorders: Theory, Research, and Treatment

Wang Z, Baker DG, Harrer J, Hamner M, Price M, Amstadter A (2011) The relationship between combat-related posttraumatic stress disorder and the 5-HTTLPR/rs25531 polymorphism. Depression and anxiety 28(12):1067–1073

Weathers FW, Ruscio AM, Keane TM (1999) Psychometric properties of nine scoring rules for the Clinician-Administered Posttraumatic Stress Disorder Scale. Psychological Assessment 11(2):124

Weathers FW, Keane TM, Davidson JR (2001) Clinician-Administered PTSD Scale: A review of the first ten years of research. Depression and anxiety 13(3):132–156

Wittchen HU (1994) Reliability and validity studies of the WHO-Composite International Diagnostic Interview (CIDI): a critical review. J Psychiatr Res 28(1):57–84

Woon FL, Sood S, Hedges DW (2010) Hippocampal volume deficits associated with exposure to psychological trauma and posttraumatic stress disorder in adults: a meta-analysis. Prog Neuropsychopharmacol Biol Psychiatry 34(7):1181–1188

Xie P, Kranzler HR, Poling J, Stein MB, Anton RF, Brady K, Gelernter J (2009) Interactive effect of stressful life events and the serotonin transporter 5-HTTLPR genotype on posttraumatic stress disorder diagnosis in 2 independent populations. Archives of general psychiatry 66(11):1201–1209

Xie P, Kranzler HR, Poling J, Stein MB, Anton RF, Farrer LA, Gelernter J (2010) Interaction of FKBP5 with childhood adversity on risk for post-traumatic stress disorder. Neuropsychopharmacology 35(8):1684–1692

Xie P, Kranzler HR, Yang C, Zhao H, Farrer LA, Gelernter J (2013) Genome-wide association study identifies new susceptibility loci for posttraumatic stress disorder. Biol Psychiatry 74:656–663

Yehuda R, Bierer LM (2009) The relevance of epigenetics to PTSD: Implications for the DSM-V. J Trauma Stress 22(5):427–434

Yehuda R, Southwick SM, Nussbaum G, Wahby V, Giller EL Jr, Mason JW (1990) Low urinary cortisol excretion in patients with posttraumatic stress disorder. J Nerv Ment Dis 178(6): 366–369

Yehuda R, Koenen KC, Galea S, Flory JD (2011) The role of genes in defining a molecular biology of PTSD. Dis Markers 30(2):67–76

Young EA, Kornstein SG, Marcus SM, Harvey AT, Warden D, Wisniewski SR, John Rush A (2009) Sex differences in response to citalopram: a STAR* D report. J Psychiatr Res 43(5): 503–511

Young-Wolff KC, Chereji E, Prescott CA (2012) Heritability of alcohol dependence is similar in women and men. Evid Based Ment Health 15(3):57

Ystrom E, Reichborn-Kjennerud T, Aggen SH, Kendler KS (2011) Alcohol dependence in men: reliability and heritability. Alcohol Clin Exp Res 35(9):1716–1722

Zhang TY, Hellstrom IC, Bagot RC, Wen X, Diorio J, Meaney MJ (2010) Maternal care and DNA methylation of a glutamic acid decarboxylase 1 promoter in rat hippocampus. J Neurosci 30(39):13130–13137