REVIEW PAPER

PTSD and Sexual Dysfunction in Men and Women

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ABSTRACT

Introduction. Difficulties in sexual desire and function often occur in persons with posttraumatic stress disorder (PTSD), but many questions remain regarding the mechanisms underlying the occurrence of sexual problems in PTSD.

Aim. The aim of this review was to present a model of sexual dysfunction in PTSD underpinned by an inability to regulate and redirect the physiological arousal needed for healthy sexual function away from aversive hyperarousal and intrusive memories.

Method. A literature review pertaining to PTSD and sexual function was conducted. Evidence for the comorbidity of sexual dysfunction and PTSD is presented, and biological and psychological mechanisms that may underlie this co-occurrence are proposed.

Main Outcome Measures. This manuscript presents evidence of sexual dysfunction in conjunction with PTSD, and of the neurobiology and neuroendocrinology of PTSD and sexual function.

Results. Sexual dysfunction following trauma exposure may be mediated by PTSD-related biological, cognitive, and affective processes.

Conclusions. The treatment of PTSD must include attention to sexual dysfunction and vice versa. **Yehuda R, Lehrner A, and Rosenbaum TY. PTSD and sexual dysfunction in men and women. J Sex Med 2015;12:1107–1119.**

Key Words. Sexual Dysfunction; Posttraumatic Stress Disorder; Neurobiology; Neuroendocrinology

Introduction

Although sexual dysfunction is not a specific symptom of posttraumatic stress disorder (PTSD), it is a frequent clinical complaint among trauma survivors [1–6]. PTSD is a stress-related condition that occurs following exposure to an extremely traumatic event, with an estimated population lifetime prevalence of 5.7% for men and 12.8% for women [7]. A traumatic event is defined in the Diagnostic and Statistical Manual of Mental Disorders (DSM 5 [8]) as involving exposure to actual or threatened death, serious injury, or sexual violence. Even indirect exposure, such as witnessing or learning of a trauma to a loved one, can induce PTSD. Four symptom clusters have been defined in the recently revised DSM 5 [8]. (i) Intrusion symptoms include recurrent and unwanted memories, nightmares, flashbacks, and intense distress or physiological reactivity after exposure to traumatic reminders. (ii) Avoidance symptoms reflect effortful avoidance of trauma-related thoughts, feelings, or reminders. (iii) Negative alterations in cognitions or mood may include persistent negative beliefs about oneself or the world, negative emotions related to the trauma (such as guilt, shame, anger, horror), loss of interest in significant activities, feelings of alienation from others, and an inability to experience positive or loving emotions. (iv) Alterations in arousal and reactivity include irritability or aggression, self-destructive or reckless behavior, hypervigilance, exaggerated startle response, and problems with concentration and sleep. For a PTSD diagnosis,

symptoms must persist for at least a month following trauma exposure and cause clinically significant distress or functional impairment.

Symptoms of PTSD may interfere across the continuum of sexual behavior, including desire, arousal, activity, consummation, and satisfaction. For example, persons with PTSD may actively avoid sexual activity to minimize feelings of physical arousal or vulnerability that could trigger flashbacks or intrusive memories [9,10]. Because some symptoms of PTSD, such as nightmares, intrusive memories, and insomnia, are so distressing and result in such great restrictions in overall quality of life, sexual dysfunction is often not presented as a top priority by treatment-seeking patients. Trauma specialists may not inquire about their patients' sexual lives because they are unaware of the comorbidity of sexual dysfunction and PTSD, or because they fear that the treatment of sexual issues requires specific expertise outside of their purview.

Recent developments in PTSD neurobiological research now permit a discussion of the role of PTSD pathophysiology in sexual problems. Neuroanatomical circuits and neurochemical and endocrinological processes disrupted in PTSD are critical to those involved in all aspects of sexual behavior including desire, arousal, and orgasm (e.g., Zoladz and Diamond [11]). In this article, we suggest that sexual difficulties in PTSD occur because of an inability to regulate and redirect the physiological arousal needed for healthy sexual function away from hyperarousal and aggression circuits. This is because the very hormonal and neural circuit activation that normally leads to positively valenced sexual arousal and activity is already overactive in PTSD, but leads to anxiety, fear, and other PTSD symptoms. The pairing of physiological arousal with fear or horror may override healthy sexual functioning, so that arousal signals impending threat rather than pleasure. If the biology of PTSD primes an individual to associate arousal with trauma-associated threat, guilt, or shame, or impairs the ability to downregulate or contain the fear response, the biological cards may be stacked against sexual function and intimacy in PTSD by impeding the inhibitory neurobiological processes required for sexual activity. Specific mechanisms are described below.

Sexual Dysfunction in PTSD

Until recently, sexual dysfunction has been linked with exposure to sexual trauma rather than to the presence of PTSD or PTSD pathophysiology [12,13]. Studies of nonsexual trauma including combat, accidents, and criminal victimization have now also established an association with sexual dysfunction in men and women including sexual desire, arousal, orgasm, activity, and satisfaction (e.g., Letourneau et al. and other several studies [9,14–16]). Table 1 provides a review of the literature on sexual dysfunction in PTSD, showing that PTSD, rather than trauma exposure per se, is the more proximal antecedent to sexual problems. Sexual dysfunction is greater in exposed persons with PTSD, compared with similarly exposed survivors without, regardless of the nature of the trauma [1,9,21,22,26]. In a random, nonclinical sample of women, PTSD accounted for significant variance in sexual dysfunction outcomes (odds ratio = 2.3) after accounting for history of crime victimization, rape, injury during the crime, and depression [9]. The association has been explored in more detail in combat veterans. For example, a study of male combat-exposed veterans (n = 90) found overall rates of erectile dysfunction of 85% in veterans with PTSD compared with 22% in veterans without PTSD [1].

Interpretation of studies of sexual dysfunction in veterans has been complicated by participant age and length of disorder confounds, but more recent studies with veterans of wars in Iraq, Afghanistan, and Croatia document that sexual dysfunction is common even among relatively young combat veterans with PTSD [4,17]. For example, a recent study of 367 male active duty personnel and recent veterans aged 40 and under found that probable PTSD (as assessed by self-report) increased the likelihood of erectile dysfunction 30-fold and sexual dysfunction 6-fold, a greater increase than that associated with depression [28]. Sexual problems were also associated with reduced quality of life and lower happiness scores. Larger chart review studies have supported these findings. Among 4,755 male Afghanistan and Iraq veterans who sought treatment from Veterans Affairs medical centers, PTSD was a significant risk factor for sexual dysfunction for younger (<40 years) as well as older (>40 years) veterans [23]. A large, retrospective record review of 405,275 male Afghanistan and Iraq veterans (median age = 28) who were followed for at least 2 years found that veterans with PTSD were more likely to have sexual dysfunction and/or prescriptions for medications that treat sexual dysfunction (10.6%), compared with those with any other mental health diagnosis (7.2%) or no diagnosis (2.3%) [19]. After controlling for potentially

Table 1 PTSD and sexual dysfunction literature review

Study	Sample	Relevant assessment measures	Relevant findings
Anticevic and Britvic [17]	Croatia 101 male war veterans with PTSD and 55 healthy male control volunteers (not combat exposed) receiving outpatient general health care	M-PTSD CAPS 30-item structured questionnaire (validated in a Croatian population sample) assessing sexual functioning	War veterans with PTSD had less sexual activity, hypoactive sexual desire, and erectile difficulties, lower frequency of sexual fantasies, foreplay, oral sex, and sexual intercourse than controls. Among veterans with PTSD, antidepressant use was associated with less frequent masturbation and sexual desire, and less frequent premature ejaculation.
Arbanas [18]	Croatia 5 groups of male combat veterans with Criterion A trauma, living with same sexual partner for 6 months, receiving outpatient MH treatment (n = 164): 1. PTSD+, SSRI– (n = 38) 2. PTSD+, SSRI+ (n = 50) 3. Subthreshold PTSD, SSRI– (n = 21) 4. Subthreshold PTSD, SSRI+ (n = 30) 5. PTSD– (n = 25)	SCID MMPI-2 CAPS IIEF	PTSD+ reported less sexual desire than PTSD–.* PTSD+ and subthreshold PTSD showed no differences in SD. Subthreshold PTSD, SSRI+ had less SD than PTSD+, SSRI+.
Breyer et al. [19]	United States 405,275 male OEF/OIF veterans who used VA healthcare and had 2-year follow-up, divided into 3 groups: 1. MH diagnosis– 2. MH diagnosis+, PTSD– 3. PTSD+ (with or without other MH diagnosis)	Retrospective chart review to identify: • Diagnoses representing male SD • Prescription in chart for medication to treat ED and other SD	PTSD+ more likely to have SD, prescription, or both (10.6%) compared with other two groups. PTSD increased risk of SD more than threefold (ARR = 3.61, 95% CI = 3.48–3.75). PTSD and psychiatric meds had highest risk of SD (ARR = 4.59, 95% CI = 4.41–4.77).
Cohen et al. [20]	United States 71,504 female OEF/OIF veterans	Chart review of VA data from veterans who were new users of VA healthcare from October 7, 2001, through December 31, 2010	Likelihood of sexual dysfunction increased: PTSD+/depression- (adjusted OR = 6.78) PTSD–/depression+ (adjusted OR = 7.55) PTSD+/depression+ (adjusted OR = 10.24)
Cook et al. [21]	United States 331 male World War II military POWs, married or living with a partner, who completed screening and follow-up procedures	POW Trauma Index PCL DAS PAIR: assesses emotional, social, sexual, intellectual, and recreational aspects of intimacy CPQ-S	Ex-POWs with PTSD more likely to report problems with intimacy on PAIR. Emotional numbing significantly associated with intimacy independent of other PTSD symptom clusters.
Cosgrove et al. [1]	United States 1. 44 male combat veterans receiving treatment in outpatient VA PTSD clinic 2. 46 controls (male patients receiving outpatient medical care at same VA)	DSM-IV PTSD diagnosis on the basis of a "clinical diagnostic interview conducted by an experienced clinician" PCL CES IIEF	Veterans with PTSD had lower total IIEF scores compared with controls. These participants had lower overall satisfaction and orgasmic function, and showed trends toward lower intercourse satisfaction and erectile function. No difference in sexual desire was observed. Eighty-five percent of veterans with PTSD had ED compared with only 22% of the control group ($P < 0.05$). Forty-five percent of the patients with PTSD had moderate to severe ED compared with only 13% of the controls ($P = 0.023$). The severity of PTSD correlated significantly with the total IIEF scores ($P < 0.001$) and the EF ($P < 0.001$), orgasmic function ($P = 0.001$), sexual desire ($P = 0.025$), intercourse satisfaction ($P < 0.001$), and overall satisfaction ($P < 0.001$) domains.†
Dekel and Solomon [22]	Israel 25 ex-POWs with PTSD 85 ex-POWs with no PTSD 104 control veterans	DAS ISS	Ex-POWs with PTSD had lower sexual satisfaction.

Table 1 Continued

Study	Sample	Relevant assessment measures	Relevant findings
Helmer et al. [5]	United States The first 158 consecutive OEF/OIF patients seen for an initial assessment in a VAMC post-deployment clinic	Retrospective chart review from initial clinic visit to 6 months later (180 days) to assess: sexual health issues, patient factors, PTSD (based on score of 2 or higher on Primary Care PTSD screening instrument).	Bivariate relationships between any sexual problem and: being female (OR = 3.9), probable PTSD (OR = 2.4), depression (OR = 3.8), SSRI/SNRI Rx (OR = 3.2), black race (OR = 2.2), and age 30–39 (OR = 3.52). Alcohol use and TBI were not associated with sexual problems.
Hirsch [4]	United States 53 male OEF/OIF veterans in inpatient PTSD treatment	Chart review of routine clinical assessment at intake of: libido, erectile function, and ejaculatory function Only symptoms predating treatment with psychiatric meds were included for analysis	Approximately 74% reported diminished libido (with and without a partner) (n = 39) 49% reported ED (n = 26) 15% reported ED (n = 8)
Hosain et al. [23]	United States 4,755 Iraqi/Afghanistani veterans who sought treatment at VA inpatient or outpatient clinics from September 2007 and August 2009	Chart review of routinely collected administrative data (ICD codes and medications)	PTSD was a risk factor for sexual dysfunction in younger veterans aged < 40 years (OR = 1.18) and in older veterans > 40 years (OR = 2.14).
Kaplan [6]	United States Vietnamese veterans with PTSD in inpatient psychiatric unit at VA hospital	Clinical case report	31-year-old veteran with severe PTSD presented with comorbid ED, and was successfully treated with his wife using "behavioral/psychodynamic sex therapy techniques." A "number of other patients" approached the author with similar complaints, only raising the issue when they learned of an "approachable" provided who had experience treating sexual dysfunction.
Kotler et al. [24]	Israel 3 groups: 1. PTSD+, SSRI– (n = 15) 2. PTSD+, SSRI+ (n = 27) 3. Healthy controls (n = 49)	Impact of Event Scale (IES) SCL-90 18-item questionnaire on sexual functioning (SF)‡	15 of 18 SF items predicted by PTSD (covering desire, arousal, orgasm, activity, satisfaction). PTSD+, SSRI+ showed more SD on 7 items (covering desire, arousal, frequency of activity with a partner). In PTSD + group, high correlation of anger/hostility on SCL-90 and SD in items related to sex with a partner.
Letourneau et al. [9]	United States 391 women drawn from a larger household probability sample, divided based on presence (n = 228) or absence (n = 165) of sexual problems	IRI Modified DIS including items developed to assess PTSD using DSM-III criteria and to assess sexual problems	The presence of PTSD contributed significantly to the variance (adjusted OR = 2.30) after accounting for history of criminal victimization, completed rape, physical injury during the crime, and depression.
Letourneau et al. [2]	United States 90 male (primarily Vietnam era) veterans with combat-related PTSD in outpatient treatment at VA PTSD clinic	GRISS PTSD diagnosis based on chart review and structured diagnostic interview (either CAPS-1 or SCID-III-R)	82% scored 5 or higher on the GRISS, indicating a sexual problem. Elevations on subscales: impotence problem (69%), premature ejaculation (50%), "nonsensuality scale" indicating sexual disinterest (44%), avoidance of sexual interactions (48%), dissatisfaction subscale (33%), noncommunication subscale (41%), infrequency subscale (73%). No demographic variables correlated with GRISS subscale scores.
McDevitt-Murphy et al. [16]	United States 62 trauma-exposed women; 16 PTSD +	Sexual functioning: TSI Dysfunctional Sexual Behavior (DSB) and Sexual Concerns (SC) Scales CAPS	No differences in DSB and SC Scales between PTSD+ and PTSD–. SC and DSB associated with numbing; SC also associated with hyperarousal.

Table 1 Continued

Study	Sample	Relevant assessment measures	Relevant findings
Nunnink et al. [10]	U.S. OEF/OIF veterans 197 veterans with trauma exposure newly enrolling for VA care	Sexual functioning: one item regarding "impotence or other sexual problems" in a medical symptom checklist; and an item asking whether the veteran had a current diagnosis related to "diminished sexual desire or function." Davidson Trauma Scale (to assess PTSD), with three symptoms representing the construct of numbing extracted from the avoidance cluster	Those reporting sexual problems reported greater PTSD symptom severity. Of the PTSD symptom clusters, only the numbing cluster was a significant predictor of sexual functioning.
Öznur et al. [25]	Turkey 25-year-old male presenting with PTSD symptoms and concurrent spontaneous erections and ejaculations 2–3 times/day	Case report SCID IES BDI	Re-experiencing and hyperarousal symptoms hypothesized to have led to increased adrenergic system activation with resultant spontaneous ejaculation without sexual stimulus. Treatment with paroxetine reduced PTSD symptom severity and decreased frequency of spontaneous erection and ejaculation.
Riggs et al. [26]	United States 50 male Vietnamese veterans in heterosexual relationships and their female partners	DAS MSI RPS FIS PCL-M	Couples with PTSD had more difficulties with intimacy; men had more difficulty than female partners with intimacy Emotional numbing significantly predicted veteran's FIS scores.
Schnurr et al. [27]	United States 242 female active duty and veterans with PTSD in PTSD treatment study	CAPS Sexual functioning: TSI DSB and SC Scales	Numbing and hyperarousal symptoms associated with both scales; re-experiencing associated only with dysfunctional sexual behaviors. Posttreatment recovery was associated with lower scores on SC scale, no change in DSB.
Solursh and Solursh [3]	United States Unmedicated male veterans (primarily Vietnam era) in PTSD inpatient unit	Clinical impressions	Estimated reports by veterans of failing to "achieve or maintain erection or premature ejaculation" at over 80%.
Wilcox et al. [28]	United States 367 male active duty service members and recent veterans, ≤ age 40.	IIEF ASES-M PCL-M	Probable PTSD increased the likelihood of erectile dysfunction (OR = 29.48) and sexual dysfunction (OR = 6.03), a greater increase than that associated with mild depression.
Zerach et al. [14]	Israel 105 ex-POWs and 94 control veterans from 1973 Yom Kippur War, married or living with female partners	PTSD Inventory "Intimate partner questionnaire" to assess "Capacity for Intimacy" DAS ISS	Ex-POWs had lower sexual satisfaction scores. PTSD symptoms had negative relationship with sexual satisfaction. Marital intimacy partly mediated relationship of PTSD with sexual satisfaction.

*Data analysis did not covary for age although age was reported to be associated with sexual functioning scores in the sample.
†PTSD patients had much higher psychiatric medication use, which could affect findings.
‡Questionnaire apparently developed for the study, no reliability or validity data provided.
ASES-M = Arizona Sexual Experiences Scale—Male; ARR = adjusted risk ratio; BDI = Beck Depression Inventory; CAPS = Clinician-Administered PTSD Scale; CES = Combat Exposure Scale; CI = confidence interval CPQ-S = Communications Pattern Questionnaire-Short Form; DAS = Dyadic Adjustment Scale; DIS = Diagnostic Interview Schedule; DSM = Diagnostic and Statistical Manual of Mental; Disorders ED = erectile dysfunction; EF = Erectile Function, an indicator of erectile dysfunction; FIS = Fear of Intimacy Scale; GRISS = Golombok-Rust Inventory of Sexual Satisfaction; ICD = International Classification of Diseases; IIEF = International Index of Erectile Function; IRI = Incident Report Interview; ISS = Index of Sexual Satisfaction; MH = mental health; MMPI-2 = Minnesota Multiphasic Personality Inventory-2; M-PTSD = Mississippi Scale for Combat-Related PTSD; MSI = Marital Status Inventory; OEF = Operation Enduring Freedom; OIF = Operation Iraqi Freedom; OR = odds ratio; PAIR = Personal Assessment of Intimacy in Relationships; PCL = PTSD Checklist for DSM-IV; PCL-M = PTSD Checklist-Military; POW = prisoner of war; PTSD = posttraumatic stress disorder; RPS = Relationship Problems Scale; SCL-90 = Symptom Checklist 90; SCID = Structured Clinical Interview for DSM Disorders; SD = sexual dysfunction; SSRI = selective serotonin reuptake inhibitor; TBI = traumatic brain injury; TSI = Trauma Symptom Inventory; VA = Veterans Affairs; VAMC = Veteran's Affairs Medical Center.

confounding variables (e.g., sociodemographic, military service, comorbid disease, and opioid medication), PTSD increased the risk of sexual dysfunction by more than threefold (adjusted risk ratio = 3.61, 95% confidence interval = 3.48–3.75).

Chart review studies have the strength of large sample sizes, but they are limited by the data in the medical records entered to document routine clinical care and not gathered for research purposes. Furthermore, even when sexual difficulties are documented in some way, it is important to understand their etiology in a trauma survivor with PTSD. Sexual interest, desire, functioning, and satisfaction may be influenced differently by depressive PTSD symptoms such as numbing and anhedonia vs. hyperarousal. Furthermore, it is sometimes the case that trauma survivors express sexual difficulties with intimate partners, but report no difficulties in achieving orgasm through masturbation or with a stranger (e.g., Hirsch [4]). It is possible that different types of sexual problems in PTSD are mediated by different biological and psychological processes.

For combat veterans, sexual difficulties in intimate relationships may relate to specifics of combat experiences or enduring emotional sequelae of combat such as guilt, horror, and shame. For example, the intense physiological arousal and emotions experienced when under fire, and when killing others, may include excitement, pleasure, and exhilaration and have been described as a "combat high," which may be followed by feelings of guilt and shame [29,30]. The association of aggression and violence with sex has long been observed, from physical anthropology to cultural studies to popular media and advertising. Grossman's monograph [29] on the psychological costs of killing includes a trenchant description of the parallels between killing and sex, and research on this topic with veterans begs exploration of these themes.

Animal models have also documented effects of traumatization on sexual behavior. For example, decreased sexual motivation and increased anxiety following exposure to a contextual traumatic reminder thought to simulate intrusive memories seen in PTSD have been shown in different strains of laboratory rats [31], suggesting that memory of a traumatic experience impairs sexual function. In both studies, latency to achieve the first mount, but not latency to first intromission, ejaculation, or post-ejaculation intermission, was significantly increased in stressed rats compared with non-stressed rats.

Biology of PTSD

PTSD reflects a condition in which the body's natural homeostatic mechanisms for recovery have failed, resulting in a prolonged state of sympathetic nervous system (SNS) arousal [32]. Normally, when confronting a threat, the SNS engages the body's "fight or flight" response [33]. SNS activation results in the release of adrenaline and glucose, increased heart rate and blood pressure, and restricted blood flow to the genitals. The threat response also includes the parasympathetic nervous system (PNS), associated with containment of the stress response and activities when the body is at rest. Activation of the hypothalamic–pituitary–adrenal (HPA) axis leads to release of cortisol from the adrenal glands, which ultimately facilitates the containment of the stress response through negative feedback inhibition. Thus, among other things, increased cortisol levels following threat help to inhibit the SNS and restore physiological homeostasis [33].

Cortisol levels have been reported to be lower in chronic PTSD [11,34], but also immediately following trauma exposure in persons who are at greater risk of PTSD or who later develop PTSD [35,36]. The reduced cortisol activity at the time of the trauma is thought to facilitate a prolonged SNS response [32]. Lower than optimal cortisol levels may prevent inhibition of norepinephrine (NE) and lead to increased levels of catecholamines. Thus, a negative feedback loop may develop where heightened catecholamine levels (such as NE or adrenaline) or heightened sensitivity to catecholamines perpetuates anxious arousal [32] so that the trauma survivor remains more aroused for a longer period of time. In a study of rape victims evaluated hours post-rape, cortisol and levels of the NE metabolite 3-methoxy-4-hydroxyphenylglycol (MHPG) were inversely related [37]. Increased levels of NE have also been associated with chronic PTSD, particularly in men [38]. Furthermore, combat veterans with PTSD show an increased response to yohimbine [39–41]. Yohimbine is a naturally occurring alkaloid with stimulant and aphrodisiac effects that has been shown to enhance desire, arousal, and sexual performance [42]. It is a selective pre-synaptic alpha-2 receptor antagonist on noradrenergic neurons, and is associated with an increase in sympathetic nerve activity and NE. Yohimbine is used as an over-the-counter herbal remedy for erectile dysfunction. In PTSD, however, yohimbine was shown to result in panic and flashbacks [43]. In

fact, the investigation of the effects of yohimbine in PTSD was prompted by a case report of a PTSD patient who reported a flashback after its use. Thus, from the perspective of arousal, PTSD patients seem to have naturally high levels of hormones associated with the physiology of arousal and even hyperarousal.

Physical arousal related to elevated catecholamines such as NE has been linked to the formation of traumatic memories. Heightened autonomic arousal has been theorized to result in an "overconsolidation" of traumatic memories such that the memories are not only overdetermined, but emotionally distressing [44,45]. Testosterone has also been linked with contextual fear conditioning [46]. In mice, castration-induced loss of testosterone caused a significant reduction of contextual fear memory [47]. Despite the belief among some PTSD patients that low testosterone levels are related to their sexual dysfunction, testosterone has been shown to be higher in combat veterans with PTSD compared with those with depression and normal controls [48].

In terms of neural circuitry, there is evidence from brain imaging studies that the amygdala, a brain region critical in fear response, may be more reactive to fear-inducing stimuli among those with PTSD [11,49]. Positron emission tomography and magnetic resonance imaging studies consistently document that the region that normally inhibits the amygdala, the anterior cingulate, shows reduced activity in PTSD [50]. Dysfunctional anterior cingulate activity might result in a failure to contain activation of the amygdala, leading to a hyperreactive limbic system in PTSD [11]. Individuals with PTSD have shown a stronger auditory startle response, which failed to habituate across trials, compared with those who were trauma exposed but without PTSD [51]. These neurobiological networks in PTSD link physiological arousal with fear and danger. Thus, in PTSD, there is less suppression and containment of hormonal and neural systems underlying states of arousal, and these systems appear to be highly relevant for symptoms such as hypervigilance, agitated hyperarousal, and intrusive traumatic memories.

Biology of Sexual Function

The hormonal and neuronal networks activated in PTSD are also those engaged in normative sexual desire and behavior. Sexual stimuli activate the SNS, increasing oxygen uptake and blood flow from the heart, and the PNS, increasing blood flow to the genitals. However, healthy sexual functioning requires an optimal level of SNS activation; if such activation is above or below the threshold, sexual function may be impaired [52].

Sexual stimuli generally produce a decrease in cortisol, and the decrease is associated with sexual desire [53]. In a nonclinical sample, women who demonstrated increased salivary cortisol in response to sexual stimuli reported less subjective arousal and desire and lower sexual satisfaction than those whose cortisol declined [54]. Higher cortisol response following sexual stimuli has also been associated with sexual anxiety [55]. Cushing syndrome, a condition of hypercortisolism, is associated with decreased libido in men and women [56]. Men with psychogenic erectile dysfunction have also demonstrated high levels of cortisol and anxiety [56].

Other relevant hormones and neurotransmitters for sexual desire, arousal, and behavior include testosterone, NE, and oxytocin. Testosterone levels are elevated in preparation for and during sexual activity, and withdrawal of testosterone in men results in a significant decrease in sexual desire and activity [56]. Cortisol release following an acute stressor has been associated with decreased testosterone in men [57]. There is a wide range of testosterone levels in healthy adult males, and these normal variations do not appear to drive differences in libido or performance. Findings regarding testosterone in women have been inconsistent; however, this hormone also plays a role in female sexual function and treatment with testosterone has been found to improve sexual function in women with low desire and/or arousal [58]. Plasma NE increases during sexual arousal and activity in men and women, increasing up to 12-fold at orgasm in men [56]. Oxytocin is a neuropeptide hormone released during sexual arousal and orgasm in men and women. Higher levels of oxytocin have been associated with higher orgasm intensity [56]. Oxytocin has been linked to positive affect, bonding, trust, empathy, and romantic attachment and may thus also play an indirect role in libido [56,59]. Oxytocin also has an anxiolytic effect, reducing anxiety in a fear-potentiated startle paradigm [60]. Increased levels of oxytocin suppress both sympathetic arousal and HPA-axis responses to stress [61].

Sexual stimuli also produce brain responses in the ventral striatum, the amygdala, the anterior cingulate cortex, and the orbitofrontal cortex, which underlie sexual "wanting" or interest, rather than sexual arousal or consummation [62]. Sexual

consummation involves a distinct network and shifts in brain region activity. For example, amygdala activity decreases as sexual activity progresses. Areas within the medial temporal lobe and ventromedial prefrontal cortex are also downregulated during sexually pleasurable activity [62]. Neuroimaging studies demonstrate that hyposexual patients appear to have heightened activity in the sexual interest network (including the amygdala and ventral prefrontal cortex) but are unable to switch to brain regions associated with the sexual consummation network (including ventral pallidum, posterior insula, and middle cingulated cortex) [62].

Inhibition of sexual response may be context dependent (e.g., in the face of an immediate threat) or more chronic, suggestive of a generalized inhibited state (such as induced by chronic stress) [63]. Less is known about the neurochemical mechanisms of sexual inhibition, but opioids, endocannabinoids, and serotonin have all been implicated [62]. Abuse of opioid narcotics is known to cause sexual problems, including decreased desire, erectile dysfunction, and increased ejaculation latency [64], although the role of endogenous opiates is less clear [56]. Stress-induced opioid activation leads to sexual inhibition in animal models [65]. Increased cortisol has been associated with decreased perceptions of desire, arousal, and satisfaction, but not genital arousal, in response to sexual stimuli in women, as described above [54].

Competing Biology: PTSD and Sexual Desire and Activity

The biological processes involved in sexual desire, arousal, and activity thus engage many of the same hormonal and neurological networks as PTSD (see Figure 1). But whereas PTSD and sexual activity both involve physiological arousal, healthy sexual functioning also requires inhibition of fear and threat networks. The hyperactive threat response system characteristic of PTSD may impair healthy sexual functioning. For example, in the absence of PTSD, catecholamines such as NE are positively associated with sexual arousal and activity [66]. However, NE works in a curvilinear fashion such that moderate elevations support optimal sexual behavior but high levels produce a generalized fear response that is sexually inhibitory. It is for this reason that yohimbine, which increases NE, can be conducive to sexual functioning in persons without PTSD, but induce panic attacks and flashbacks in individuals with PTSD as noted above [39]. The

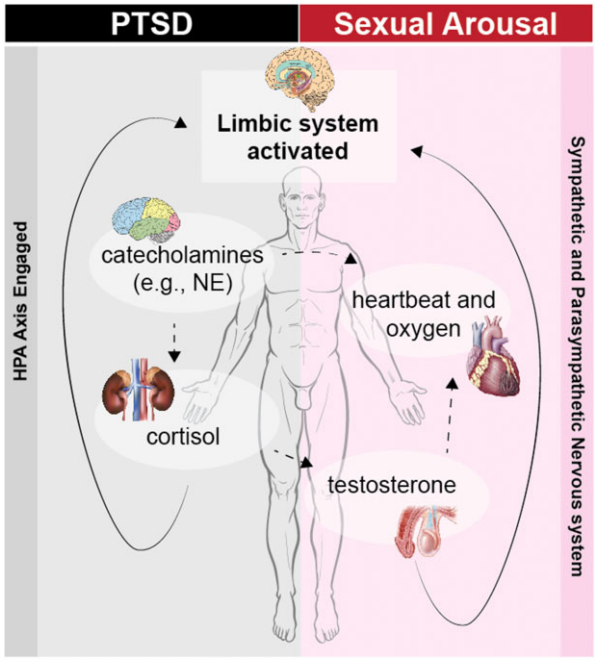

Figure 1 Biological systems engaged in posttraumatic stress disorder (PTSD) and sexual arousal
HPA = hypothalamic–pituitary–adrenal;
NE = norepinephrine

pairing of heightened catecholamines in PTSD with sexual dysfunction was recently demonstrated in an unusual case report in which a 25-year-old male patient with PTSD presented with spontaneous erections and ejaculation without sexual stimuli two to three times per day [25]. After ruling out organic causes, the patient was treated with a selective serotonin reuptake inhibitor (SSRI) (paroxetine), which successfully reduced both the PTSD and sexual symptoms. The authors hypothesize that adrenergic activation associated with escalating PTSD symptoms caused the spontaneous erections and ejaculation. Anecdotal reports of vivid intrusions of traumatic images during sexual activity [4] may also reflect a pairing of physiological arousal with danger. Correspondingly, some veterans report sexual arousal during combat that becomes paired with guilt or shame and interferes with intimacy.

Altered cortisol functioning may play a role in sexual function in PTSD by failing to contain catecholamine levels during sexual arousal. Like NE, cortisol may also have a curvilinear relationship with sexual function, such that moderate levels of cortisol (such as induced by physical exercise) may be consistent with sexual arousal, whereas high or low levels may be inhibiting [52]. Thus, sexual function involves a degree of physiological arousal

that mirrors a fear response, and in some contexts, low levels of stress or threat may even lead to sexual arousal for some [67]. However, an overreactive stress response and the inability to contain and neutralize that response may instead inhibit sexual function. Oxytocin and β-endorphin, associated with sexual arousal, consummation, and attachment, have also been found to be low in PTSD [68,69]. Together with higher testosterone in men with PTSD, the net effect of this hormone imbalance may be to increase irritability, anger, and anxiety and reduce feelings of trust and attachment which may in turn affect libido and sexual functioning.

Successful sexual activity requires the ability to dampen amygdala activation [70], but if the amygdala and other brain regions associated with fear are not adequately suppressed, as in PTSD, this may impede successful sexual engagement and consummation. Sexual dysfunction in PTSD may reflect the brain's difficulty "switching gears" as both hormonal and neuronal pathways work together to prevent extinction of the fear-related memory. Cortical brain areas interpret previously neutral stimuli such as physiological arousal (now paired with traumatic reminders) as dangerous. This may make it difficult for a PTSD patient to recalibrate and view the physical arousal associated with sexual activity as safe, because arousal has now become a deeply conserved sign of threat.

Competing Phenomenology: PTSD and Sexual Desire and Activity

Models of sexual function must consider cognitive and affective processes as well as biological ones. Many PTSD symptoms are incompatible with feelings of pleasure, intimacy, trust, and safety. Individuals with PTSD may avoid intimacy because it raises feelings of emotional vulnerability, necessitates some degree of physical vulnerability, or is incompatible with constant hypervigilance. For trauma survivors with PTSD, the relinquishing of control necessary to achieve orgasm may trigger feelings of helplessness, anger, and fear such that sexual activity becomes paired with negative affect. Emotional numbing and interpersonal disconnection also run counter to sexual desire and function. The experience of emotional shutdown reported by many individuals with PTSD blocks feelings of love, attachment, and closeness. Traumatized individuals who have PTSD often develop feelings of self-blame, guilt, and shame, as well as beliefs that they are irreparably tainted or spoiled. Such altered self-schemas can contribute to fears of rejection or beliefs that the individual does not deserve love and pleasure and consequently affect sexual function. These may contribute to active avoidance of sexual intimacy, whether conscious or not.

Finally, anger and rage at partners may emerge and impair sexual function. The prominence of anger and aggressive behavior in PTSD has been recognized in the recent revision to the diagnostic criteria in the DSM-5 [8], which now include "irritable behavior and angry outbursts (with little or no provocation) typically expressed as verbal or physical aggression toward people or objects." Among men with PTSD, sexual dysfunction correlated highly with anger and hostility as assessed by the Symptom Check List-90, a self-report measure of psychological symptoms and distress [24]. Individuals may feel anger at partners for being unable to understand their experiences and symptoms, for making sexual and interpersonal demands, and for triggering the aversive thoughts and feelings associated with the trauma and PTSD. The constellation of symptoms and behaviors characteristic of PTSD often results in significant relationship discord, as evidenced by the high rates of divorce among veterans with PTSD [21].

Other Factors That May Interfere with Sexual Function

A competing explanation for the psychobiological model proposed above is that the loss of libido and sexual function seen in PTSD is a consequence of the frequently comorbid condition of depression, a secondary consequence of having a mental disorder (rather than being specific to PTSD), or is iatrogenically induced by the antidepressants commonly prescribed for PTSD and depression, and these questions remain to be more fully investigated. Currently, SSRIs are the only Food and Drug Administration-approved pharmacological treatment for PTSD, and sexual dysfunction is a well-known side effect of these medications. A study of sexual functioning in treated and untreated men with PTSD found that those with PTSD had impaired sexual functioning across all assessed domains (desire, arousal, orgasm, activity, and satisfaction) compared with healthy controls, but those treated with SSRIs reported significantly more impaired desire, arousal, and frequency of sexual activity [24]. Among male combat veterans treated with SSRIs, those with subthreshold PTSD reported better sexual functioning in all assessed domains (e.g., erectile function, orgasmic function,

desire, and satisfaction) compared with those meeting full diagnostic criteria for PTSD [18]. Combat veterans with PTSD treated with antidepressants reported less frequent masturbation than untreated veterans, suggesting that antidepressants may contribute to hypoactive sexual desire in PTSD [17]. Among male veterans with PTSD, those treated with the benzodiazepine clonazepam had greater complaints of sexual dysfunction compared with those treated with other benzodiazepines [71]. It is important to consider psychiatric comorbidities, as SSRIs may have different implications for loss of libido in the context of depression vs. PTSD. The presence of traumatic brain injury, highly comorbid with PTSD in returning veterans from Iraq and Afghanistan, may also affect sexual functioning.

In addition to pharmacotherapy, traditional sex therapy treatments might also inadvertently exacerbate problems if an underlying etiology of PTSD is undiagnosed. Treatments that do not account for PTSD may fail to recognize that sexual inhibition may be an expression of avoidance of arousal, rather than an inability to become aroused. Failing to account for the biology of PTSD may lead to treatment approaches that are in fact synergistic with PTSD pathophysiology. Most treatment approaches, however, appear compatible with treatment for PTSD (e.g., cognitive behavioral therapy, desensitization, and mindfulness).

Treatment Implications

The increasing documentation of the comorbidity of PTSD and sexual dysfunction, especially among young, otherwise healthy individuals, warrants a call for training for providers and screening for patients presenting with trauma exposure or sexual dysfunction. Treatment for either PTSD or sexual dysfunction requires careful and sensitive assessment of both domains. Given the pervasive and fundamental phenomenon of avoidance in sustaining PTSD, some patients may wish to continue to avoid sex, and may therefore not mention sexual dysfunction as a problem to their providers. It may be difficult for clinicians to distinguish low desire or inability to perform from symptoms reflecting interpersonal withdrawal or fear. Additional treatment challenges include the shame and guilt associated with both trauma and sexual dysfunction, symptoms which may be exacerbated by both experiences.

When sexual dysfunction and PTSD co-occur, it is unclear whether these problems should be treated sequentially, together, or whether treating PTSD will resolve symptoms of sexual dysfunction even if they are not a treatment target. Schnurr et al. [27] assessed sexual dissatisfaction, dysfunction, and dysfunctional sexual behavior among female veterans and active duty personnel pre- and posttreatment for PTSD. The majority of these women had histories of sexual trauma. They found significant improvement in sexual satisfaction and function among those who recovered from PTSD, but no changes in dysfunctional sexual behavior in either group.

Initial treatment recommendations for patients with comorbid PTSD and substance use disorders suggested sequential treatment of substance use first followed by trauma-focused treatment for PTSD. However, research has demonstrated the safety and efficacy of concurrent treatment [72]. If sexual intimacy touches so many core experiential aspects of PTSD, perhaps targeting sexual problems early will improve the efficacy of trauma-focused psychotherapies. A small, prospective, naturalistic study of patients with PTSD (nine men and one woman) found that adjunctive, individually designed sex therapy in addition to stable treatment for PTSD resulted in significant improvements in all domains of sexual functioning [73]. Interestingly, the addition of sex therapy also resulted in significant improvements across all domains of the Impact of Events Scale, a self-report measure that assesses intrusion and avoidance symptoms of PTSD. These improvements were found regardless of the duration or severity of PTSD or sexual dysfunction symptoms. Addressing sexual intimacy may also strengthen relationships and thus improve patients' social support, a powerful predictor of mental health and functional outcomes in PTSD [74].

PTSD and sexual dysfunction affect spouses and partners as well as the traumatized individual. Partners may assume a nonsexualized role, intuiting the implied threat of sexual activity and assuming a protective stance that facilitates avoidance of sexual behavior. They may reduce demands and take on a parentified role. Intimate partners may develop complementary clinical presentations, such as depression or anxiety disorders [75], which are also associated with problems in sexual functioning. Conversely or concomitantly, they may feel rejected, confused, and angry, leading to escalating demands or estrangement, creating further barriers to sexual intimacy. Therefore, for patients with PTSD, treatment of sexual dysfunction that involves intimate partners must take into account

the possible relationship distress often associated with PTSD. Psychoeducation for patients and their partners will likely be an important part of treatment.

Conclusion

Trauma exposure can profoundly rupture an individual's sense of safety, self-efficacy, and ability to trust and feel connected to others, features considered fundamental to healthy sexual functioning. The psychobiology of PTSD may result in an association of arousal with threat, an impaired ability to downregulate the fear response, and difficulty engaging the inhibitory neurobiological processes associated with sexual activity. Sexual arousal mimics the physiological experience of fear, and once these associations have been forged in the intense experience of trauma, it can be difficult to uncouple them.

It is not yet known whether problems with sexual function are better explained by the cognitive, emotional, and behavioral symptoms of PTSD, such as avoidance, hypervigilance, and emotional numbing, whether there is a biological component to the comorbidity, or whether there are other drivers, such as depression or medication. It is also unclear whether PTSD is associated with an overall inability to function sexually (i.e., alone, with a relative stranger), or only in the context of an affiliative, intimate relationship. Given the centrality of sexuality to interpersonal relationships and quality of life, further research on the comorbidity and treatment of sexual dysfunction and PTSD is warranted. Clinicians should assess for comorbid conditions during evaluation and treatment planning and provide education to patients and their partners.

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References

1 Cosgrove DJ, Gordon Z, Bernie JE, Hami S, Montoya D, Stein MB, Monga M. Sexual dysfunction in combat veterans with post-traumatic stress disorder. Urology 2002;60:881–4.
2 Letourneau EJ, Schewe PA, Frueh BC. Preliminary evaluation of sexual problems in combat veterans with PTSD. J Trauma Stress 1997;10:125–32.
3 Solursh LP, Solursh DS. Male erectile disorders in Vietnam combat veterans with chronic post-traumatic stress disorder. Int J Adolesc Med Health 1994;7:119–24.
4 Hirsch KA. Sexual dysfunction in male Operation Enduring Freedom/Operation Iraqi Freedom patients with severe post-traumatic stress disorder. Mil Med 2009;174:520–2.
5 Helmer DA, Beaulieu GR, Houlette C, Latini D, Goltz HH, Etienne S, Kauth M. Assessment and documentation of sexual health issues of recent combat veterans seeking VHA care. J Sex Med 2013;10:1065–73.
6 Kaplan PM. Post-traumatic stress syndrome and sexual dysfunction. J Sex Marital Ther 1989;15:74–7.
7 Kilpatrick DG, Resnick HS, Milanak ME, Miller MW, Keyes KM, Friedman MJ. National estimates of exposure to traumatic events and PTSD prevalence using DSM-IV and DSM-5 criteria. J Trauma Stress 2013;26:537–47.
8 American Psychiatric Association. Diagnostic and statistical manual of mental disorders: DSM-5. Washington, DC: American Psychiatric Publishing Incorporated; 2013.
9 Letourneau EJ, Resnick HS, Kilpatrick DG, Saunders BE, Best CL. Comorbidity of sexual problems and posttraumatic stress disorder in female crime victims. Behav Ther 1996; 27:321–36.
10 Nunnink SE, Goldwaser G, Afari N, Nievergelt CM, Baker DG. The role of emotional numbing in sexual functioning among veterans of the Iraq and Afghanistan wars. Mil Med 2010;175:424–8.
11 Zoladz PR, Diamond DM. Current status on behavioral and biological markers of PTSD: A search for clarity in a conflicting literature. Neurosci Biobehav Rev 2013;37:860–95.
12 Laumann EO, Paik A, Rosen RC. Sexual dysfunction in the United States: Prevalence and predictors. JAMA 1999; 281:537–44.
13 Najman JM, Dunne MP, Purdie DM, Boyle FM, Coxeter PD. Sexual abuse in childhood and sexual dysfunction in adulthood: An Australian population-based study. Arch Sex Behav 2005; 34:517–26.
14 Zerach G, Anat BD, Solomon Z, Heruti R. Posttraumatic symptoms, marital intimacy, dyadic adjustment, and sexual satisfaction among ex-prisoners of war. J Sex Med 2010;7:2739–49.
15 Silva PD. Sexual consequences of non-sexual trauma. Sex Marital Ther 1999;14:143–50.

16 McDevitt-Murphy ME, Weathers FW, Adkins JW. The use of the trauma symptom inventory in the assessment of PTSD symptoms. J Trauma Stress 2005;18:63–7.
17 Anticevic V, Britvic D. Sexual functioning in war veterans with posttraumatic stress disorder. Croat Med J 2008;49:499–505.
18 Arbanas G. Does post-traumatic stress disorder carry a higher risk of sexual dysfunctions? J Sex Med 2010;7:1816–21.
19 Breyer BN, Cohen BE, Bertenthal D, Rosen RC, Neylan TC, Seal KH. Sexual dysfunction in male Iraq and Afghanistan war veterans: Association with posttraumatic stress disorder and other combat-related mental health disorders: A population-based cohort study. J Sex Med 2014;11:75–83.
20 Cohen BE, Maguen S, Bertenthal D, Shi Y, Jacoby V, Seal KH. Reproductive and other health outcomes in Iraq and Afghanistan women veterans using VA health care: Association with mental health diagnoses. Womens Health Issues 2012;22:e461–71.
21 Cook JM, Riggs DS, Thompson R, Coyne JC, Sheikh JI. Posttraumatic stress disorder and current relationship functioning among World War II ex-prisoners of war. J Fam Psychol 2004;18:36–45.
22 Dekel R, Solomon Z. Marital relations among former prisoners of war: Contribution of posttraumatic stress disorder, aggression, and sexual satisfaction. J Fam Psychol 2006;20:709–12.
23 Hosain GM, Latini DM, Kauth M, Goltz HH, Helmer DA. Sexual dysfunction among male veterans returning from Iraq and Afghanistan: Prevalence and correlates. J Sex Med 2013;10:516–23.
24 Kotler M, Cohen H, Aizenberg D, Matar M, Loewenthal U, Kaplan Z, Miodownik H, Zemishlany Z. Sexual dysfunction in male posttraumatic stress disorder patients. Psychother Psychosom 2000;69:309–15.
25 Öznur T, Akarsu S, Karaahmetoğlu B, Doruk A. A rare symptom in posttraumatic stress disorder: Spontaneous ejaculation. Am J Case Rep 2014;15:69–73.
26 Riggs DS, Byrne CA, Weathers FW, Litz BT. The quality of the intimate relationships of male Vietnam veterans: Problems associated with posttraumatic stress disorder. J Trauma Stress 1998;11:87–101.
27 Schnurr PP, Lunney CA, Forshay E, Thurston VL, Chow BK, Resick PA, Foa EB. Sexual function outcomes in women treated for posttraumatic stress disorder. J Womens Health (Larchmt) 2009;18:1549–57.
28 Wilcox SL, Redmond S, Hassan AM. Sexual functioning in military personnel: Preliminary estimates and predictors. J Sex Med 2014;11:2537–45.
29 Grossman D. On killing: The psychological cost of learning to kill in war and society. Revised Edition. New York: Back Bay Books/Little, Brown and Company; 1995.
30 Solursh LP. Combat addiction: Overview of implications in symptom maintenance and treatment planning. J Trauma Stress 1989;2:451–62.
31 Hawley WR, Grissom EM, Belkin MN, James TF, Dohanich GP. Decreased sexual motivation and heightened anxiety in male Long-Evans rats are correlated with the memory for a traumatic event. Arch Sex Behav 2013;42:659–68.
32 Yehuda R. Status of glucocorticoid alterations in post-traumatic stress disorder. Ann N Y Acad Sci 2009;1179:56–69.
33 de Kloet ER, Joels M, Holsboer F. Stress and the brain: From adaptation to disease. Nat Rev Neurosci 2005;6:463–75.
34 Yehuda R. Current status of cortisol findings in post-traumatic stress disorder. Psychiatr Clin North Am 2002;25:341–68, vii.
35 Yehuda R, McFarlane AC, Shalev AY. Predicting the development of posttraumatic stress disorder from the acute response to a traumatic event. Biol Psychiatry 1998;44:1305–13.
36 Delahanty DL, Raimonde AJ, Spoonster E. Initial posttraumatic urinary cortisol levels predict subsequent PTSD symptoms in motor vehicle accident victims. Biol Psychiatry 2000;48:940–7.
37 Yehuda R, Resnick HS, Schmeidler J, Yang RK, Pitman RK. Predictors of cortisol and 3-methoxy-4-hydroxyphenylglycol responses in the acute aftermath of rape. Biol Psychiatry 1998;43:855–9.
38 Geracioti TD Jr, Baker DG, Ekhator NN, West SA, Hill KK, Bruce AB, Schmidt D, Rounds-Kugler B, Yehuda R, Keck PE Jr, Kasckow JW. CSF norepinephrine concentrations in posttraumatic stress disorder. Am J Psychiatry 2001;158:1227–30.
39 Southwick SM, Morgan CA 3rd, Charney DS, High JR. Yohimbine use in a natural setting: Effects on posttraumatic stress disorder. Biol Psychiatry 1999;46:442–4.
40 Morgan CA 3rd, Grillon C, Southwick SM, Nagy LM, Davis M, Krystal JH, Charney DS. Yohimbine facilitated acoustic startle in combat veterans with post-traumatic stress disorder. Psychopharmacology (Berl) 1995;117:466–71.
41 Bremner JD, Innis RB, Ng CK, Staib LH, Salomon RM, Bronen RA, Duncan J, Southwick SM, Krystal JH, Rich D, Zubal G, Dey H, Soufer R, Charney DS. Positron emission tomography measurement of cerebral metabolic correlates of yohimbine administration in combat-related posttraumatic stress disorder. Arch Gen Psychiatry 1997;54:246–54.
42 Allard J, Giuliano F. Central nervous system agents in the treatment of erectile dysfunction: How do they work? Curr Urol Rep 2001;2:488–94.
43 Southwick SM, Krystal JH, Morgan CA, Johnson D, Nagy LM, Nicolaou A, Heninger GR, Charney DS. Abnormal noradrenergic function in posttraumatic stress disorder. Arch Gen Psychiatry 1993;50:266–74.
44 Pitman RK. Post-traumatic stress disorder, hormones, and memory. Biol Psychiatry 1989;26:221–3.
45 Debiec J, Bush DE, LeDoux JE. Noradrenergic enhancement of reconsolidation in the amygdala impairs extinction of conditioned fear in rats–a possible mechanism for the persistence of traumatic memories in PTSD. Depress Anxiety 2011;28:186–93.
46 Edinger KL, Lee B, Frye CA. Mnemonic effects of testosterone and its 5alpha-reduced metabolites in the conditioned fear and inhibitory avoidance tasks. Pharmacol Biochem Behav 2004;78:559–68.
47 McDermott CM, Liu D, Schrader LA. Role of gonadal hormones in anxiety and fear memory formation and inhibition in male mice. Physiol Behav 2012;105:1168–74.
48 Karlovic D, Serretti A, Marcinko D, Martinac M, Silic A, Katinic K. Serum testosterone concentration in combat-related chronic posttraumatic stress disorder. Neuropsychobiology 2012;65:90–5.
49 Simmons AN, Matthews SC, Strigo IA, Baker DG, Donovan HK, Motezadi A, Stein MB, Paulus MP. Altered amygdala activation during face processing in Iraqi and Afghanistani war veterans. Biol Mood Anxiety Disord 2011;1:6.
50 Shin LM, Whalen PJ, Pitman RK, Bush G, Macklin ML, Lasko NB, Orr SP, McInerney SC, Rauch SL. An fMRI study of anterior cingulate function in posttraumatic stress disorder. Biol Psychiatry 2001;50:932–42.
51 Shalev AY, Peri T, Orr SP, Bonne O, Pitman RK. Auditory startle responses in help-seeking trauma survivors. Psychiatry Res 1997;69:1–7.
52 Lorenz TA, Harte CB, Hamilton LD, Meston CM. Evidence for a curvilinear relationship between sympathetic nervous system activation and women's physiological sexual arousal. Psychophysiology 2012;49:111–7.
53 van Anders SM, Brotto L, Farrell J, Yule M. Associations among physiological and subjective sexual response, sexual

desire, and salivary steroid hormones in healthy premenopausal women. J Sex Med 2009;6:739–51.
54 Hamilton LD, Rellini AH, Meston CM. Cortisol, sexual arousal, and affect in response to sexual stimuli. J Sex Med 2008;5:2111–8.
55 Heiman JR, Rowland DL, Hatch JP, Gladue BA. Psychophysiological and endocrine responses to sexual arousal in women. Arch Sex Behav 1991;20:171–86.
56 Meston CM, Frohlich PF. The neurobiology of sexual function. Arch Gen Psychiatry 2000;57:1012–30.
57 Chatterton RT Jr, Vogelsong KM, Lu YC, Hudgens GA. Hormonal responses to psychological stress in men preparing for skydiving. J Clin Endocrinol Metab 1997;82:2503–9.
58 Davis SR, Braunstein GD. Efficacy and safety of testosterone in the management of hypoactive sexual desire disorder in postmenopausal women. J Sex Med 2012;9:1134–48.
59 Marazziti D, Dell'Osso B, Baroni S, Mungai F, Catena M, Rucci P, Albanese F, Giannaccini G, Betti L, Fabbrini L, Italiani P, Del Debbio A, Lucacchini A, Dell'Osso L. A relationship between oxytocin and anxiety of romantic attachment. Clin Pract Epidemiol Ment Health 2006;2:28.
60 Missig G, Ayers LW, Schulkin J, Rosen JB. Oxytocin reduces background anxiety in a fear-potentiated startle paradigm. Neuropsychopharmacology 2010;35:2607–16.
61 Cohen H, Kaplan Z, Kozlovsky N, Gidron Y, Matar MA, Zohar J. Hippocampal microinfusion of oxytocin attenuates the behavioural response to stress by means of dynamic interplay with the glucocorticoid-catecholamine responses. J Neuroendocrinol 2010;22:889–904.
62 Georgiadis JR, Kringelbach ML, Pfaus JG. Sex for fun: A synthesis of human and animal neurobiology. Nat Rev Urol 2012;9:486–98.
63 Bancroft J, Janssen E. The dual control model of male sexual response: A theoretical approach to centrally mediated erectile dysfunction. Neurosci Biobehav Rev 2000;24:571–9.
64 Bang-Ping J. Sexual dysfunction in men who abuse illicit drugs: A preliminary report. J Sex Med 2009;6:1072–80.
65 Pfaus JG, Wilkins MF. A novel environment disrupts copulation in sexually naive but not experienced male rats: Reversal with naloxone. Physiol Behav 1995;57:1045–9.
66 Kruger THC, Haake P, Chereath D, Knapp W, Janssen OE, Exton MS, Schedlowski M, Hartmann U. Specificity of the neuroendocrine response to orgasm during sexual arousal in men. J Endocrinol 2003;177:57–64.
67 Barlow DH, Sakheim DK, Beck JG. Anxiety increases sexual arousal. J Abnorm Psychol 1983;92:49–54.
68 Hoffman L, Burges Watson P, Wilson G, Montgomery J. Low plasma beta-endorphin in post-traumatic stress disorder. Aust N Z J Psychiatry 1989;23:269–73.
69 Olff M. Bonding after trauma: On the role of social support and the oxytocin system in traumatic stress. Eur J Psychotraumatol 2012;3:18597. doi: 10.3402/ejpt.v3i0.18597.
70 Pfaus JG. Pathways of sexual desire. J Sex Med 2009;6:1506–33.
71 Fossey MD, Hamner MB. Clonazepam-related sexual dysfunction in male veterans with PTSD. Anxiety 1994;1:233–6.
72 Mills KL, Teesson M, Back SE, Brady KT, Baker AL, Hopwood S, Sannibale C, Barrett EL, Merz S, Rosenfeld J, Ewer PL. Integrated exposure-based therapy for co-occurring posttraumatic stress disorder and substance dependence: A randomized controlled trial. JAMA 2012;308:690–9.
73 Chudakov B, Cohen H, Matar MA, Kaplan Z. A naturalistic prospective open study of the effects of adjunctive therapy of sexual dysfunction in chronic PTSD patients. Isr J Psychiatry Relat Sci 2008;45:26–32.
74 Ozer EJ, Best SR, Lipsey TL, Weiss DS. Predictors of posttraumatic stress disorder and symptoms in adults: A meta-analysis. Psychol Bull 2003;129:52–73.
75 Yambo T, Johnson M. An integrative review of the mental health of partners of veterans with combat-related posttraumatic stress disorder. J Am Psychiatr Nurses Assoc 2014;20:31–41.