Mechanisms Underlying Sexual Violence Exposure and Psychosocial Sequelae: A Theoretical and Empirical Review

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Sexual violence is associated with a range of negative mental health and behavioral sequelae, including posttraumatic stress disorder (PTSD), depression, substance abuse/dependence, risky sexual behavior, and interpersonal relationship problems. However, mechanisms underlying these associations are not well understood. Identifying mechanisms that explain linkages between sexual violence and poor outcomes is of paramount importance in determining when and how to intervene to prevent or reduce the magnitude of these outcomes. This review focuses on theories that have been proposed to explain risk of negative outcomes among sexual violence victims, including the development of traumagenic dynamics and emotion dysregulation. We also review promising biological mechanisms that may explain the risk of negative outcomes among sexual violence victims, including studies concerned with epigenetic and neurobiological mechanisms.

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Sexual violence encompasses the experience of rape (i.e., forcible or drug- or alcohol-facilitated penetration) and sexual assault (i.e., unwanted sexual contact accomplished using force, drug or alcohol facilitation, or coercion). An unfortunately common experience for U.S. adults, rape is reported by nearly one in five women and one in 71 men throughout their lifetimes (Black et al., 2011). The current review will summarize the prevalence, burden, and consequences of sexual trauma as well as mechanisms that explain relations between sexual trauma exposure and psychosocial sequelae.

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PREVALENCE OF SEXUAL VIOLENCE

Recent estimates from the Centers for Disease Control suggest that 18.3% of U.S. adult women and 1.4% of U.S. adult men report attempted or completed rape, including drug- or alcohol-facilitated penetration, during their lifetimes (Black et al., 2011). These estimates are consistent with the 20% of women identified as victims of sexual assault in prior national surveys (Elliott, Mok, & Briere, 2004; Koss, Gidycz, & Wisniewski, 1987). Black and colleagues also found that 44.6% of women and 22.2% of men reported experiencing other sexual violence, including sexual coercion and unwanted sexual contact. Although sexual violence can occur at any point in the lifecourse, national crime victim reports indicate that the age ranges of 11–24 are associated with the highest risk of exposure to sexual violence (Kilpatrick, Edmunds, & Seymour, 1992). Sexual violence also disproportionately affects girls and women, with female victims

reporting more than 90% of all sexual assaults (Pimlott-Kubiak & Cortina, 2003).

PUBLIC HEALTH BURDEN

The public health costs of sexual assault are substantial. A study of the tangible and intangible costs of sexual violence in the state of Michigan found that rape and sexual assault cost the state nearly $7 billion in 1996 (Post, Mezey, Maxwell, & Wibert, 2002). Consistent with other studies (Dolan, Loomes, Peasgood, & Tsuchiya, 2005), intangible costs (e.g., decreased quality of life) accounted for the majority of these estimates. However, tangible costs (e.g., police, medical, mental health, and victim advocate services) also contributed to these figures. These exorbitant costs to society emphasize the public health importance of better understanding mechanisms underlying relations between sexual violence and negative sequelae to develop more effective interventions.

SEQUELAE OF SEXUAL VIOLENCE

Sexual violence has long been recognized as a precursor to a wide range of negative outcomes (Ullman & Brecklin, 2003), although we acknowledge that not all victims develop such outcomes (e.g., Breslau et al., 1998; Kessler, Sonnega, Bromet, Hughes, & Nelson, 1995). The present review will be organized around the most studied consequences of sexual violence: psychopathology, risk behaviors, and interpersonal/intrapersonal problems.

The three most widely studied mental health consequences are posttraumatic stress disorder (PTSD), major depressive disorder (MDD), and substance use disorders (SUDs). PTSD, a disorder that requires exposure to a traumatic event and is characterized by intrusive trauma-related recollections, avoidance of people, places, thoughts, and emotions associated with the trauma, and heightened general arousal, including irritability and sleep difficulties (American Psychiatric Association [APA], 1994), is the most commonly reported mental disorder associated with sexual violence exposure. Among representative samples of adolescent, college, and adult household-residing women, the lifetime prevalence of PTSD associated with sexual violence ranges from 26.6% to 45.2% (Walsh et al., 2012). Prospective, longitudinal studies of abused and neglected children have shown that female children, particularly those with sexual abuse histories, report a higher prevalence of PTSD in adulthood when compared with male children (Koenen & Widom, 2009). Often comorbid with PTSD (e.g., Kessler et al., 2003), MDD is characterized by chronic low mood, anhedonia, and feelings of worthlessness and hopelessness (American Psychiatric Association, 1994). Among representative samples of college and adult community-residing women, 40% of sexual violence victims report a lifetime diagnosis of MDD (Kilpatrick, Resnick, Ruggiero, Conoscenti, & McCauley, 2007). Substance abuse, a diagnosis that reflects persistent substance use despite disruptions in social or occupational functioning (APA, 1994), is comorbid with PTSD in 36–50% of substance abuse treatment-seeking cases (Brady, Back, & Coffey, 2004). Among representative samples of adolescents, the prevalence of substance abuse and dependence among sexual assault victims ranges from 5% for hard drug abuse and dependence to 11% for marijuana abuse and dependence to 13% for alcohol abuse and dependence (Kilpatrick et al., 2000). One form of alcohol abuse, binge drinking, has been identified as especially problematic among college victims of sexual violence, with estimates of monthly binge drinking ranging from 28% to 42% (Kilpatrick et al., 2007).

Sexual violence victims also may engage in a number of risky behaviors that are of public health relevance, including sexual activity with a greater number of sexual partners, having more frequent unprotected sexual encounters, and trading sex for goods and services more often, when compared with those without sexual abuse histories (Senn, Carey, & Coury-Doniger, 2011). Prospective, longitudinal studies of substantiated cases of child abuse and maltreatment reveal that abused children are at greater risk of promiscuity, prostitution, and HIV in adulthood (Widom & Kuhns, 1996; Wilson & Widom, 2008). Sexual violence victims also report more sexual partners, unwanted pregnancies, abortions, and sexually transmitted infections relative to nonvictims (van Roode, Dickson, Herbison, & Paul, 2009). Sexual risk behaviors also have been observed among victims globally (e.g., Olley, 2008).

Although the responsibility for an assault lies with the perpetrator alone, engagement in substance abuse

and sexual risk behaviors can increase risk of repeated sexual violence exposure, a phenomenon termed *revictimization* (see Classen, Palesh, & Aggarwal, 2005). Meta-analyses suggest a medium to large effect size ($r = 0.59$) for the association between early sexual abuse and revictimization, with stronger effect sizes for more severe forms of victimization (i.e., penetration; Roodman & Clum, 2001). Further, according to the National Intimate Partner and Sexual Violence Survey, 35.2% of women who reported a completed rape before the age of 18 experienced a completed rape as an adult (Black et al., 2011). When defined as experiencing two or more distinct sexual assaults regardless of developmental period, more than 50% of adolescent, college, and adult household-residing women with victimization histories report revictimization (Walsh et al., 2012). Thus, even among those younger than 18, repeated sexual violence exposure may have already occurred.

Beyond this increased risk of revictimization, sexual violence victims report more problems in other aspects of interpersonal relationships, including having less emotional trust in their intimate partners and viewing their partners as less reliable in following through with important aspects of the relationship (DiLillo & Long, 1999; Mullen, Martin, Anderson, Romans, & Herbison, 1994). Sexual violence victims also report greater sexual difficulties with intimate partners, including less frequent sexual activity (Dennerstein, Guthrie, & Alford, 2004), lower sexual satisfaction and sexual drive (Randolph & Reddy, 2006), and greater negative affect while sexually aroused (Schloredt & Heiman, 2003). Sexual violence victims also are more likely to report psychological, physical, and sexual victimization by an intimate partner (e.g., DiLillo, Giuffre, Tremblay, & Peterson, 2001; Whitfield, Anda, Dube, & Felitti, 2003).

INTERPERSONAL AND INTRAPERSONAL MECHANISMS

Several mechanisms have been proposed to explain relations between sexual violence exposure and negative outcomes. Although the present review will focus on biological mechanisms that have been implicated in these relations, interpersonal and psychological processes are also likely to play a role in determining the range of negative outcomes observed.

For example, a number of investigations have studied the impact of disclosure and the reactions received from others on adjustment following sexual violence. Adult women who disclose their sexual violence experiences less than one month following the abuse or assault are significantly less likely to develop PTSD and MDD (Ruggiero et al., 2004). Relative to those who do disclose, nondisclosers are more likely to have PTSD and MDD. However, perceived support in response to such a disclosure is also important in predicting outcomes (Littleton, 2010). For instance, negative responses (e.g., blaming or not believing the victim) are associated with poorer outcomes, including increased problem drinking, particularly for women with limited social support (Ullman, Starzynski, Long, Mason, & Long, 2008). In considering outcomes, however, it is important to account for the type of disclosure support source, as reports to formal support sources (e.g., police) are much more likely to be perceived as drawing negative reactions relative to more informal sources (e.g., friends, family; Ahrens, Campbell, Ternier-Thames, Wasco, & Sefl, 2007).

According to Finkelhor and Browne's (1985) traumagenic dynamics theory, experiencing sexual abuse at the hands of a trusted adult or caregiver can negatively shape a child's perception of his- or herself, his or her behavior, and his or her interpersonal relationships, through four mechanisms: traumatic sexualization, betrayal, shame/guilt, and powerlessness. Traumatic sexualization, which refers to learning that sexual activities can be used to obtain affection and rewards, may translate into sexual risk taking and promiscuity among victims. As a result of experiencing abuse by a trusted adult or caregiver, victims also may develop a sense of betrayal and problems with trust that can pervade other important interpersonal relationships. Shame or guilt may arise due to stigmatization associated with being part of an activity viewed as deviant by society. Finally, as a result of being unable to stop the abuse as it was occurring, victims may internalize a sense of powerlessness that can manifest as lack of assertiveness, decreased agency in other important relationships, and increased risk of symptoms of depression.

Applying this theory to women attending a sexually transmitted disease clinic, researchers have found that women with childhood sexual abuse (CSA) histories

report higher levels of traumatic sexualization, powerlessness, unprotected sex, a greater number of sex partners, and more sex trading when compared with nonvictims (Senn et al., 2011). Further, schemas regarding rejection that develop in the wake of child abuse and maltreatment have been shown to explain relations between abuse and a greater number of consensual sexual partners (Roemmele & Messman-Moore, 2011), and these maladaptive sexual schemas may increase risk of sexual assault (revictimization) during adolescence (Niehaus, Jackson, & Davies, 2010). Prospective, longitudinal studies suggest that victims also are at greater risk of unstable romantic relationships (e.g., characterized by infidelity, walking out on a partner) during adolescence, which in turn predicts risky sexual behavior in adulthood (Wilson & Widom, 2011).

Emotional dysregulation, conceptualized as a multifaceted construct reflecting difficulties identifying, modulating, and expressing emotional states (Gratz & Roemer, 2004; Gross, 1998), also has been hypothesized to play a role in predicting negative outcomes among sexual violence victims. Uncontrollable and unpredictable sexual violence may undermine the development of adaptive emotion regulation abilities by triggering conditioned and unconditioned emotions, including fear and arousal (Marx, Heidt, & Gold, 2005). Victims reared in families in which abuse is occurring may have few opportunities to observe and model effective emotion regulation abilities and thus may have few resources available to modulate chronic, high levels of negative affect. To cope, they may become emotionally or experientially avoidant, and when avoidance does not effectively ameliorate distress, victims may develop emotion-related psychopathology (e.g., PTSD, MDD) and seek external coping mechanisms including substance abuse and risky sexual behavior (Polusny & Follette, 1995), which is consistent with the self-medication hypothesis of substance abuse (Khantzian, 1997).

Support for emotion regulation and maladaptive coping or self-medication as explanatory mechanisms in the link between sexual violence and negative sequelae stems from research documenting that emotion dysregulation underlies PTSD and MDD (e.g., Tull et al., 2007), and victims report greater use of substances to reduce both negative affect (Grayson & Nolen-Hoeksema, 2005) and assault-related PTSD symptoms (Miranda, Meyerson, Long, Marx, & Simpson, 2002; Ullman, Filipas, Townsend, & Starsynski, 2005). Hyperarousal symptoms, in particular, are associated with increased alcohol and drug use and dependence (Dixon, Leen-Feldner, Ham, Feldner, & Lewis, 2009; Reed, Anthony, & Breslau, 2007; Saladin, Brady, Dansky, & Kilpatrick, 1995), 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).

Conceptualized as a tension-reduction behavior, sexual violence victims also report engaging in more frequent risky sexual behavior to reduce negative affect (Orcutt, Cooper, & Garcia, 2005) or regulate emotional states (Messman-Moore, Walsh, & DiLillo, 2010). Orcutt et al. (2005) suggest that victims may seek physical intimacy to increase positive affect and decrease negative affect, but because they fear the vulnerability that accompanies emotional intimacy with a single partner, they may engage in sexual relationships with a greater number of partners. Engaging in sex to accomplish nonsexual goals (e.g., negative affect reduction) can have negative health and relationship consequences for victims (for review, see Crepaz & Marks, 2001). Further, sex with a greater number of partners may increase risk of sexual revictimization possibly by increasing the likelihood of encountering a sexually aggressive partner (Merrill et al., 1999).

In addition to their independent contributions, intrapersonal and interpersonal processes also may operate in concert to increase the likelihood of negative sequelae. For instance, substance abuse and dependence are highly comorbid with risky sexual behavior (Cavazos-Rehg et al., 2007; Randolph & Mosack, 2006), and intoxicated women with sexual abuse histories are more likely to report that they would engage in unprotected sex during laboratory vignette studies when compared with sober and nonvictimized women (Schacht et al., 2010). Sexual violence victims with PTSD are more likely to abuse substances to cope with distress (Miranda et al., 2002; Ullman et al., 2005), and postassault substance abuse has been shown to predict increases in risky sexual behavior (Deliramich & Gray,

2008). Sexual violence victims also may use substances to reduce fear or anxiety around engaging in sexual activity (Sanjuan, Langenbucher, & Labouvie, 2009). However, substance abuse while engaging in sexual behavior may increase risk of revictimization, perhaps by suggesting vulnerability to a potential perpetrator or by impeding the ability to detect threat and respond defensively when an interaction becomes risky (Marx et al., 2005; Messman-Moore & Long, 2002).

BIOLOGICAL MECHANISMS LINKING SEXUAL VIOLENCE TO ADVERSE CONSEQUENCES

Several previous reviews have described the role of genetic variation in the development of PTSD and associated diagnoses (e.g., Broekman, Olff, & Boer, 2007; Koenen, Amstadter, & Nugent, 2009). The current review is intended to examine the biological mechanisms via which sexual violence gives rise to negative sequelae. We focus on three areas: epigenetics, neuroimaging, and neuroendocrine studies.

Epigenetic Modifications

Epigenetic mechanisms refer to heritable modifications in gene expression or functionality that do not involve changes to the underlying DNA sequence. Although multiple epigenetic mechanisms exist (e.g., noncoding RNA, histone modification), DNA methylation has been the most widely studied with regard to trauma exposure and PTSD and MDD. DNA methylation involves the addition of a methyl group to the five position of the cytosine pyrimidine ring or the number six nitrogen of the adenine purine ring. Animal studies have demonstrated that maternal care early in life can influence DNA methylation and stress responses in offspring that are sustained into adult life (Weaver et al., 2004, 2005). Animal models of PTSD in particular have revealed increased DNA methylation in the hippocampus among those exposed to a psychosocial stress regimen (Cherktow-Deutsher, Cohen, Klein, & Ben-Shachar, 2010; Mahan et al., 2012; Roth, Zoladz, Sweatt, & Diamond, 2011; Zhang et al., 2010), suggesting that environmental stressors can give rise to enduring epigenetic changes. Animal studies also suggest that these epigenetic modifications can be passed to offspring (e.g., Franklin et al., 2010).

Epigenetic modifications may be one mechanism through which trauma exposure leads to adverse outcomes (see Table 1). Childhood trauma exposure, including sexual abuse, has been associated with methylation in specific genes, including the promoter region of the serotonin transporter (Beach, Brody, Todorov, Gunter, & Philibert, 2010, 2011; Smith et al., 2011). Epigenetic modifications associated with childhood trauma exposure have been examined in relation to

Table 1. Epigenetic mechanisms implicated in PTSD, MDD, SUDs, and risky sexual behavior

Study	Participants	Findings
Beach et al. (2011)	155 women adopted as children	Methylation in the 5HTT promoter region mediates associations between CSA and antisocial behavior
Beach et al. (2010)	96 male and 96 female participants adopted as children	Child abuse is associated with increased SLC6A4 methylation
Koenen et al. (2011)	100 urban-dwelling adults	SLC6A4 methylation moderated the relation between number of traumatic events and PTSD after controlling for the SLC6A4 genotype
Labonte et al. (2012)	Suicide completers and natural deaths	Childhood abuse associated with methylation of hippocampal glucocorticoid receptor variants
Smith et al. (2011)	25 childhood trauma +PTSD; 25 childhood trauma −PTSD; 26 controls with PTSD; 26 controls without PTSD	Global methylation elevated in PTSD participants; CpG sites in several genes also differentially methylated among those with PTSD; plasma cytokine levels associated with PTSD, childhood trauma, and total life stress
Uddin et al. (2010)	100 urban-dwelling adults	Unmethylated immune-related genes associated with increased immune dysfunction among PTSD relative to non-PTSD individuals
Uddin et al. (2011)	100 urban-dwelling adults	Greater MAN2C1 methylation interacts with exposure to more traumatic events to predict higher likelihood of PTSD
van IJzendoorn et al. (2010)	143 men and women adopted as children	Methylation in 5HTT promoter associated with maladaptive responses to loss or other traumas in the ll variant; the ss variant of 5HTT predicted greater maladaptive responses to loss or other traumas when lower levels of methylation were present

Note: CSA = childhood sexual abuse; PTSD = posttraumatic stress disorder; MDD = major depressive disorder; SUD = substance use disorder.

adverse outcomes including adult antisocial behavior and suicide completion (Beach et al., 2011; Labonte et al., 2012). Furthermore, microarray methylation studies have identified differences in methylation patterns for individuals with and without PTSD and MDD (Fuchikami et al., 2011; Smith et al., 2011; Uddin et al., 2010; Uddin et al., 2011). Although research in this area is nascent, there are indications that epigenetic signatures associated with exposure to environmental stressors such as sexual violence may influence the development of disease processes including PTSD and MDD.

Structural and Functional Neurological Changes

Approximately 20 articles published with data from human subjects between 1992 and 2012 were identified via PsycINFO and Medline using search terms including "sexual abuse," "sexual assault," "brain," "fMRI," "hippocampus," "amygdala," and "prefrontal cortex" (see Table 2).

Of the 20 studies reviewed here, nine were brain-imaging studies that focused on associations between sexual violence exposure and structural abnormalities in the brain. A number of these studies documented reduced volume in the hippocampus, a region of the brain involved in episodic memory, among sexual violence victims (Andersen et al., 2008; Bremner, Randall, Vermetten, & Staib, 1997; Bremner et al., 2003a; Stein, Yehusa, Koverola, & Hanna, 1997; Thomaes et al., 2010). However, not all studies found structural differences between victims and nonvictims (De Bellis, Hooper, Woolley, & Shenk, 2010; Landre et al., 2010; Pederson et al., 2004), and it remains unclear whether trauma exposure or the development of psychopathology following trauma exposure is predictive of differences that have been observed. For instance, Bremner et al. (2003a) found reduced hippocampal volume among sexual abuse victims only if they developed PTSD, whereas Dannlowski et al. (2012) found an association between childhood trauma exposure and diminished volume in several regions of the brain, including the hippocampus, even in the absence of PTSD. Age of sexual violence exposure also has been studied in relation to brain development, and at least one study has suggested that there may be critical "windows" of exposure associated with impaired development in certain regions of the brain (Andersen et al., 2008). For example, sexual violence exposure occurring between the ages of 3–5 and 11–13 has been associated with reduced hippocampal volume, whereas sexual violence exposure at other ages was associated with structural differences in different areas of the brain (e.g., frontal cortex; Andersen et al., 2008).

The remaining 11 studies reviewed here used functional imaging to examine activation, blood flow, and metabolism is various regions of the brain that have been associated with sexual violence exposure. Using paradigms intended to elicit emotional responses, sexual violence victims evidenced decreased blood flow (Bremner et al., 1999, 2003a, 2003b), diminished glucose metabolism (Kim et al., 2012), and dampened activation (Noll-Husson et al., 2010) in the hippocampus relative to controls. Differential brain activation patterns have emerged for other regions of the brain as well. For example, relative to healthy controls, adult women with CSA-related PTSD evidenced decreased blood flow to the orbitofrontal cortex, anterior cingulate, medial prefrontal cortex, hippocampus, and fusiform gyrus, and increased activation in the posterior cingulate, left inferior parietal cortex, left middle frontal gyrus, and visual association and motor cortex when processing emotional word pairs (Bremner et al., 2003b). Similar patterns of activation have been observed when women with CSA-related PTSD listen to personalized trauma narratives describing their own abuse experiences (Bremner et al., 1999), and dissociative responses to such trauma scripts have been associated with more activation in the superior and middle temporal gyri, the inferior frontal gyrus, occipital and parietal lobes, medial frontal gyrus, medial cortex, and anterior cingulate (Lanius et al., 2002). However, these findings of differential activation to trauma scripts appear circumscribed to victims who develop PTSD, as sexual violence victims with other diagnoses (e.g., borderline personality disorder [BPD]) do not demonstrate the same pattern of activation (Schmahl, Vermetten, Elzinga, & Bremner, 2004).

When exposed to other types of trauma-related negative stimuli (e.g., trauma-related negative emotional words), adults with histories of physical or sexual abuse demonstrate increased initial activation in the amygdala, a region of the brain involved with fear neurobiology, relative to controls (Protopopescu et al., 2005); however,

Table 2. Neurobiological mechanisms implicated in PTSD, MDD, SUDs, and risky sexual behavior

Study	Participants	Findings
Andersen et al. (2008)	26 women with CSA; 17 healthy controls	CSA occurring between ages 3–5 and 11–13 associated with reduced hippocampal volume; CSA occurring between the ages of 9 and 10 associated with reduced corpus callosum volume; and CSA occurring between the ages of 14 and 16 associated with reduced frontal cortex volume
Bremner et al. (1997)	17 adult victims of childhood physical or sexual abuse with PTSD; 17 controls	PTSD patients had smaller left hippocampal volume relative to controls
Bremner et al. (1999)	22 CSA victims with and without PTSD	CSA memories associated with increased blood flow to the anterior prefrontal cortex, posterior cingulate, and motor cortex and decreased blood flow in the right hippocampus, fusiform/inferior temporal gyrus, supramarginal gyrus, and visual association cortex in PTSD versus non-PTSD patients
Bremner et al. (2003a)	10 CSA victims with PTSD, 12 CSA victims without PTSD, and 11 women without abuse or PTSD	Women with CSA-related PTSD had smaller hippocampal volume and decreased hippocampal activation related to those with abuse and without PTSD and to nontraumatized controls
Bremner et al. (2003b)	10 women with CSA-related PTSD; 11 controls	Victims with PTSD had decreased blood flow to the orbitofrontal cortex, anterior cingulate, medial prefrontal cortex, hippocampus, and fusiform gyrus, and increased activation in the posterior cingulate, left inferior parietal cortex, left middle frontal gyrus, and visual association and motor cortex when processing emotional word pairs
Bremner et al. (2004)	12 women with CSA-related PTSD and 9 women with CSA but no PTSD	PTSD was associated with decreased blood flow in the anterior cingulate during the emotional Stroop. During the color Stroop, PTSD was associated with decreased blood flow in the visual association cortex, cuneus, and right inferior parietal lobe
Bremner et al. (2005)	8 women with CSA-related PTSD; 11 nonabused, healthy controls	PTSD was associated with left amygdala activation with fear acquisition and decreased anterior cingulate function during extinction relative to controls
Dannlowski et al. (2012)	148 healthy community participants	Childhood trauma associated with reduced volume in the hippocampus, insula, orbitofrontal cortex, anterior cingulate gyrus, and caudate
De Bellis et al. (2010)	49 maltreated children; 49 maltreated children with PTSD; 118 controls	No group differences in hippocampal volume, but decreased visual memory performance contributed to PTSD in addition to socioeconomic status and abuse characteristics
Fennema-Notestine et al. (2002)	11 IPV victims with PTSD, 11 IPV victims without PTSD, and 17 nonvictims	IPV victims have smaller supratentorial cranial vaults and smaller frontal and occipital gray matter volume relative to nonvictims
Kim et al. (2012)	12 sexually abused women with PTSD; 25 healthy controls	Glucose metabolism in left hippocampus and superior temporal and precentral gyri lower in PTSD patients relative to controls
Landre et al. (2010)	17 women with CSA-related PTSD; 17 healthy controls	PTSD women had normal global and regional brain volumes and similar cortical thickness relative to controls
Lanius et al. (2002)	7 women with CSA-related PTSD and 10 (9 female; 1 male) trauma-exposed non-PTSD	PTSD was associated with more activation in the superior and middle temporal gyri, the inferior frontal gyrus, occipital and parietal lobes, medial frontal gyrus, medial cortex, and anterior cingulate during dissociative responses to traumatic reminders
New et al. (2009)	14 with PTSD after sexual trauma, 14 with no psychiatric diagnosis after sexual trauma, and 14 nontraumatized control subjects	Sexual trauma exposure associated with less activation of the prefrontal cortex when attempting to downregulate emotional responses; however, exposed participants without PTSD had more activation in PFC when upregulating emotional responses
Noll-Husson et al. (2010)	8 sexually abused and 8 nonabused subjects	Abused subjects had greater activation in left lateral and medial superior frontal gyrus and less activation in the hippocampus during an "empathy for pain" paradigm relative to nonabused controls
Pederson et al. (2004)	17 sexually abused women with PTSD, 17 sexually abused women without PTSD, and 17 nonabused controls	No differences between groups in memory performance or hippocampal volume
Protopopescu et al. (2005)	11 sexually or physically abused men and women with PTSD; 21 nonabused controls	PTSD associated with increased initial amygdala response to trauma-related negative stimuli (but not to nontrauma-related negative stimuli) relative to controls
Schmahl et al. (2004)	20 women with physical or sexual abuse histories	In the absence of borderline personality disorder, trauma memories were associated with increased blood flow in the right dorsolateral PFC, decreased blood flow in the left PFC, and increased blood flow to the right anterior cingulate and left orbitofrontal cortex
Stein et al. (1997)	21 CSA victims; 21 nonvictims	CSA associated with reduced left hippocampal volume relative to nonvictims; reduced hippocampal volume correlated with dissociation
Thomaes et al. (2010)	31 child abuse victims with complex PTSD and 28 healthy controls	Complex PTSD associated with reduced gray matter in right hippocampus and right dorsal ACC

Note: CSA = childhood sexual abuse; PTSD = posttraumatic stress disorder; MDD = major depressive disorder; SUD = substance use disorder; IPV = interpersonal violence; PFC = prefrontal cortex; ACC = anterior cingulate cortex.

this finding does not generalize to nontrauma-related negative stimuli, perhaps because such stimuli do not activate the fear network. As evidence for this hypothesis, a study using a fear activation and extinction paradigm found that women with chronic sexual abuse–related PTSD evidence heightened amygdala activation relative to controls (Bremner et al., 2005).

Finally, in the only study that examined neural correlates of emotion regulation, sexual violence victims had greater problems recruiting the prefrontal cortex when attempting to downregulate negative emotional responses (New et al., 2009); however, victims who did not develop PTSD actually evidenced increased activation in the prefrontal cortex when attempting to upregulate positive emotions. This finding suggests that the ability to engage the prefrontal cortex and manipulate emotional states to experience more positive emotion may be a crucial factor in experiencing a more positive outcome following sexual violence exposure.

Neuroendocrine Studies

Structural and functional changes in the brain have been posited to arise from neuroendocrine responses (e.g., hypothalamic-pituitary-adrenal [HPA] axis function, locus coeruleus-noradrenergic system) to stress (see Table 3). Alterations in the HPA-axis, the primary system involved in the physiological stress response (Sapolsky, 2000), have been linked to the development and chronicity of PTSD among sexual assault victims (e.g., Yehuda, 2009). Hyperresponsivity in the HPA-axis, typically operationalized as exaggerated cortisol suppression, has been observed at rest (Cicchetti & Rogosch, 2001; Cicchetti, Rogosch, Gunnar, & Toth, 2010; Heim et al., 2009; Rinne et al., 2002; Seedat, Stein, Kennedy, & Hauger, 2003; Trickett, Noll, Susman, Shenk, & Putnam, 2010; Weissbecker, Floyd, Dedert, Salmon, & Sephton, 2006) as well as when exposed to acute stressors (i.e., in the immediate aftermath of a rape; Resnick, Yehuda, Pitman, & Foy, 1995; Yehuda et al., 1998) or a neuroendocrine challenge (Heim, Mletzko, Purselle, Musselman, & Nemeroff, 2008; Heim, Newport, Bonsall, Miller, & Nemeroff, 2001; Newport, Heim, Bonsall, Miller, & Nemeroff, 2004).

Attenuated cortisol responses with rape survivors are not entirely consistent. Although some studies have found no differences between victims and nonvictims with respect to HPA-axis function (Klumpers et al., 2004), others have found heightened daily cortisol among women with sexual abuse histories (Lemieux & Coe, 1995). A recent study of 30 war and torture-exposed individuals diagnosed with PTSD found that those with rape had increased salivary cortisol when recounting traumatic experiences (Gola et al., 2012). Further, two studies of substance-dependent treatment-seeking individuals revealed higher cortisol among sexual abuse victims during substance detoxification (Roy, 2002; Schafer et al., 2010), suggesting that the distress associated with withdrawal from cocaine and alcohol dependence may affect sexual violence victims in a biologically distinct manner from the distress associated with experiencing an additional sexual assault or rape.

Despite indications that sexual violence and other forms of abuse are associated with HPA-axis dysregulation, it remains unclear whether trauma exposure accounts for this dysregulation or whether it is a function of the development of psychopathology in the wake of a traumatic event. For instance, a study of individuals diagnosed with borderline personality disorder suggested that prolonged childhood abuse, rather than the development of associated PTSD, MDD, or even BPD symptoms was associated with hyperresponsivity in the HPA-axis (Rinne et al., 2002). As further support for the notion that abuse or trauma itself may predict HPA-axis dysregulation, Trickett et al. (2010) used prospective, longitudinal data to corroborate the pattern of lower basal cortisol among trauma-exposed individuals by studying sexual abuse victims at six assessment points from ages 6 to 30. Attenuation in cortisol was observed among adolescent victims and continued through early adulthood such that victims had significantly lower basal cortisol when compared with age-matched control participants.

Although HPA-axis function has been most commonly studied among sexual violence victims, other neuroendocrine mechanisms have been implicated in risk of negative outcomes among sexual violence victims as well. For instance, sexual and physical abuse victims with premenstrual dysphoric disorder (PMDD) have lower resting norepinephrine and greater beta-adrenergic receptor responsivity, and they also demonstrate greater norepinephrine reactivity to mental stress during the luteal phase of the menstrual cycle (Girdler

Table 3. Neuroendocrine mechanisms implicated in risk for PTSD, MDD, SUDs, and risky sexual behavior

Study	Participants	Findings
Cicchetti and Rogosch (2001)	175 maltreated children and 209 controls	Physically and sexually abused children evidenced elevations in morning cortisol; more severe sexual abuse associated with elevations in cortisol
Cicchetti et al. (2010)	265 physically or sexually abused children; 288 nonabused children	Abused children with depressive/internalizing symptoms demonstrated attenuated diurnal decrease in cortisol
Girdler et al. (2003)	28 women with PMDD; 28 women without PMDD	Sexual and physical abuse associated with lower resting norepinephrine and greater beta-adrenergic receptor responsivity among PMDD women as well as greater norepinephrine reactivity to mental stress during the luteal phase of the menstrual cycle
Gola et al. (2012)	30 war and torture victims with PTSD	Although rape victims and nonrape victims did not have different basal cortisol, salivary cortisol increased over the course of the interview for participants with rape histories relative to those without rape histories
Groer et al. (2006)	15 female rape victims; 16 controls	Rape victims had higher cytotoxic cells, lower B lymphocyte counts, higher proinflammatory biomarkers, and decreased lymphocyte proliferation compared with controls
Heim et al. (2000)	13 adult women with MDD and child sexual or physical abuse; 14 abused women without MDD; 10 with MDD and no child abuse; 12 controls	Increased pituitary-adrenal and autonomic responses to psychological stress associated with child physical or sexual abuse (particularly with MDD) when compared with controls. Women with a history of childhood abuse and MDD exhibited a more than sixfold greater ACTH response to stress than age-matched controls
Heim et al. (2002)	13 women with abuse and MDD; 14 abused, non-MDD; 10 nonabused, MDD; 12 controls	Child abuse associated with greater cortisol and ACTH responses to neuroendocrine challenge
Heim et al. (2008)	14 men with childhood abuse and no MDD; 14 men with CA and MDD; 6 men with MDD and no CA; 14 controls	CA associated with ACTH and cortisol dysregulation to dexamethasone/corticotrophin-releasing factor test; CA plus MDD associated with greatest ACTH and cortisol responses. Earlier onset, greater severity, and longer duration of abuse associated with increased responses
Heim et al. (2009)	113 adults with chronic fatigue syndrome; 124 controls	Sexual and emotional abuse associated with increased risk of CFS. Abuse interacted with CFS to predict decreased salivary cortisol after waking compared with controls
Klumpers et al. (2004)	11 women with CSA-related PTSD; 13 healthy controls	No differences in cardiovascular or neuroendocrine reactivity to physical or cognitive stress (via the orthostatic challenge and the Stroop color word test, respectively)
Lemieux and Coe (1995)	11 women with CSA-related PTSD; 9 CSA victims without PTSD; 9 nonabused controls	PTSD women had elevated daily levels of norepinephrine, epinephrine, dopamine, and cortisol
Newport et al. (2004)	19 women with child abuse; 16 women with child abuse and MDD; 10 MDD, no abuse; 19 no abuse, no MDD	Women with depression or PTSD related to abuse had greater cortisol suppression relative to healthy controls and nondepressed abuse victims
Resnick et al. (1995)	37 female rape victims	Subjects with a previous assault had lower acute cortisol immediately following the rape, but higher risk for developing PTSD at follow-up
Rinne et al. (2000)	12 BPD patients and 9 healthy controls	Higher sexual and physical abuse associated with lower prolactin
Rinne et al. (2002)	24 BPD patients with PTSD and childhood abuse; 15 BPD patients without PTSD and childhood abuse; 11 controls	Sustained childhood abuse associated with hyperresponsivity in HPA-axis rather than BPD symptoms, PTSD symptoms, or MDD symptoms
Roy (2002)	46 cocaine-dependent men in detoxification	Lower urinary-free cortisol was associated with more severe sexual abuse history. Emotional and sexual abuse both contributed to low urinary-free cortisol in multivariate analyses
Schafer et al. (2010)	38 substance abuse treatment–seeking persons	Sexual abuse was associated with higher levels of cortisol during acute withdrawal from alcohol. Childhood trauma was associated with lower ACTH after controlling for psychopathology
Seedat et al. (2003)	10 victims of physical and sexual violence with PTSD; 12 victims without PTSD; 16 nonabused controls	Physical and sexual violence associated with lower mean plasma cortisol levels relative to controls; no differences between groups in neuropeptide Y
Trickett et al. (2010)	84 sexually abused girls age 6–16; 89 controls	Attenuation of cortisol among CSA victims began in early adolescence and resulted in significantly lower basal cortisol in early adulthood
Weissbecker et al. (2006)	85 women from the community	Childhood physical and sexual abuse predicted dampened cortisol upon awakening
Yehuda et al. (1998)	20 female rape victims	Women with prior physical of sexual assault had attenuated cortisol response in the acute aftermath of rape. PTSD at 3-month follow-up not predicted by cortisol

Note: CSA = childhood sexual abuse; PTSD = posttraumatic stress disorder; MDD = major depressive disorder; SUD = substance use disorder; PMDD = premenstrual dysphoric disorder; CA = childhood abuse; CFS = chronic fatigue syndrome; BPD = borderline personality disorder; ACTH = adrenocorticotropic hormone.

et al., 2003). These findings suggest that hormones may play a role in neuroendocrine responses to stress, and these observations may be especially important among women with abuse histories. Sexual violence victims also have poorer markers of physical health and immune function, including increased level of cytotoxic cells, lower B lymphocyte counts, higher proinflammatory biomarkers, and decreased lymphocyte proliferation compared with controls (Groer, Thomas, Evans, Helton, & Weldon, 2006).

SUMMARY AND CONCLUSIONS

Numerous studies have demonstrated associations between sexual violence and a wide range of negative mental health and behavioral sequelae, including PTSD, MDD, substance abuse/dependence, risky sexual behavior, sexual revictimization, and poor interpersonal relationships. Although these outcomes have each been independently identified as important public health problems that are associated with lower quality of life, poor physical health, increased mental health-care utilization, and decreased employment (Haagsma et al., 2012; Livingston, 2009), only a small number of studies have examined comorbidity among sexual violence victims (e.g., Danielson et al., 2006; Kilpatrick et al., 2003), and we are aware of none that have comprehensively assessed all of these important sequelae within the same study. Consequently, few evidence-based assessments and interventions have been developed to measure and treat the varied clinical presentations associated with sexual violence. Based on these observations, our recommendations for studying the consequences of sexual trauma are threefold:

1. Studies should attempt to comprehensively assess independent and comorbid problems within and across each of these separate but related domains of functioning (e.g., psychopathology, risky behaviors, and interpersonal relationships).
2. Prevalence estimates of comorbid problems should be examined among sexual violence victims to clarify the proportion of victims who may be in need of services that target more than one adverse outcome. Epidemiological research also will illuminate the specific combinations of negative consequences that are most commonly observed to enable clinical researchers to develop targeted interventions that will apply most broadly to the victims presenting for treatment.
3. Studies should attempt to better understand temporal relationships between psychopathology, risky behaviors, and interpersonal problems among victims to gain insight regarding how to blend existing evidence-based interventions for individual problems into cohesive treatments that can target multiple outcomes.

The literature on mechanisms that account for associations between sexual violence exposure and psychosocial problems also could be advanced. For example, researchers and clinicians may conceptualize the negative outcomes reviewed here as distinct processes when they may, in fact, share a common etiology. We highlighted theories suggesting that emotion dysregulation may account for varied negative outcomes among sexual trauma victims (Marx et al., 2005; Polusny & Follette, 1995). If empirical studies support this assertion, emotion dysregulation may be a plausible, parsimonious intervention target, and treatments designed to address facets of emotion dysregulation that are particularly relevant to sexual trauma victims may impact problems across multiple domains of functioning.

Second, studies should build and test more comprehensive models of the complex pathways to adverse sequelae among sexual violence victims that incorporate methods from various disciplines. For example, although several psychological (e.g., emotional dysregulation) and biological (e.g., neuroendocrine dysregulation) processes have been associated with sexual violence exposure, such mechanisms are often not considered concomitantly. Better understanding the complex pathways that underlie these relations is of paramount importance to identifying those most at risk of problems and more effectively tailoring interventions to prevent or reduce the magnitude of such problems. Thus, similar to New et al. (2009), researchers should continue developing innovative translational paradigms to measure interactions between psychological and biological mechanisms in predicting adverse outcomes. These translational studies should attempt to include longitudinal follow-up data, as many of the biological mechanisms associated with sexual violence have only been studied using cross-sectional

designs, limiting the conclusions that can be drawn about the mediational role of such mechanisms.

In summary, to improve our knowledge and understanding of pathways to negative outcomes among sexual violence victims, there is a clear need to integrate findings from psychological, epidemiological, and biological perspectives into more comprehensive translational models.

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