Intimacy Post-Injury

Combat Trauma and Sexual Health

ELSPETH CAMERON RITCHIE

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ROLE OF THE SYMPATHETIC NERVOUS SYSTEM IN POST-TRAUMATIC STRESS DISORDER–RELATED MALE SEXUAL DYSFUNCTION

CLINICAL EVIDENCE AND RELATED INTERVENTIONS

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SEXUAL DYSFUNCTION AND POST-TRAUMATIC STRESS DISORDER

Severe post-traumatic stress disorder (PTSD) is sufficient in and of itself to directly engender clinically significant sexual dysfunction of sufficient severity as to impair quality of life, as opposed to requiring other, additional factors, such as age, other health concerns, chronicity of PTSD symptoms, or lifestyle. A study by Hirsch (2009) reported that over 80% of the study's combat veteran patients "were experiencing clinically relevant sexual difficulties" (Hirsch, 2009). This PTSD-related sexual dysfunction seems to be persistent, as Gruden and Gruden (2000) concluded that, without effective intervention, only 15% of the reported cases of sexual dysfunction are self-limiting (Gruden & Gruden, 2000). A study of Vietnam veterans showed that the three catecholamines: dopamine, norepinephrine (NE), and epinephrine—were all excreted at an elevated rate in patients with severe PTSD (Yehuda & Southwick, 1992). Yehuda et al. went on to note that levels of these three catecholamines seem to be particularly related to intrusive symptoms, which may contribute to the phenomenon reported by patients who experienced intrusive images during sexual relations (Yehuda & Southwick, 1992). Available evidence suggests that, at a minimum characteristics of PTSD such as autonomic arousal, anger/hostility, and relationship difficulties may contribute to the observed sexual dysfunction. The anger regulation deficits have been demonstrated in combat-related PTSD (Chemtob & Gross, 1997).

SYMPATHETIC SYSTEM ACTIVATION AND PTSD

The sympathetic nervous system (SNS) is part of the autonomic nervous system. Its role is to mobilize the body's resources under stress, to induce the fight-or-flight

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response. It is also constantly active at a basal level in order to maintain homeostasis. In PTSD, the SNS is chronically activated above the normal baseline levels (Lemieux & Coe, 1995). In large part, the activation of the SNS is accomplished by the increase of catecholamines, mainly epinephrine and NE. The role of NE in the brain is that of a neurotransmitter leading to arousal, selective attention, and vigilance, which has been demonstrated in preclinical studies (Southwick et al., 1999). Specifically, elevated urinary NE has been identified among patients with PTSD (Mason & Giller, 1988). Similarly, NE concentrations in cerebrospinal fluid (CSF) are significantly higher in subjects with PTSD than among healthy controls and have been correlated with the severity of PTSD symptoms (Geracioti et al., 2001). Such notable increases in noradrenergic activity among subjects with PTSD suggest that reducing central nervous system (CNS) noradrenergic activity could be effective in reducing the symptoms of PTSD, especially arousal symptoms, such as nightmares and startle reactions (Taylor et al., 2006).

INVASIVE TREATMENT OF SNS OVERACTIVATION

Treatments of physiological hyperarousal are available by utilizing minimally invasive modulation of the SNS. The first example of selective sympathetic modulation as a PTSD treatment was endoscopic sympathetic block (ESB) at the second thoracic vertebra (T2) done by clipping the sympathetic ganglia and was published by Dr Telaranta in 1998 (Telaranta, 1998). In a follow-up publication, Telaranta (2003) noted the similarity in features between social phobias and PTSD—especially those caused by an overactive SNS, such as heart racing, hypervigilance, and avoidance of emotionaly painful situations. ESB requires a relatively invasive surgical technique, fortunately, it seems possible to achieve similar results reported by Dr Telaranta by using stellate ganglion block (SGB), a common anesthetic procedure that is much less invasive. Early results of this SGB as utilized for treating PTSD are very promising, with success rates of from 70% to 75% and very high compliance and acceptance.

The first report of successful treatment of PTSD by SGB was published in 2008 (Lipov et al., 2008). SGB involves injecting a local anesthetic into the anterior-lateral aspect of the cervical spine, at the level of sixth cervical vertebra (C6) on the right, with the intent of anesthetizing the cervical sympathetic ganglia. To date, over 2,500 SGB's have been performed for PTSD, with no long-term adverse reactions reported. The published success rates of SGB in treating PTSD are 75% (n = 24; Navaie et al., 2014) and greater than 70% (n = 166; Mulvaney et al., 2014).

The clinical changes noted following SGB often include a marked reduction of hypervigilance, improved sleep, and reduced reactivity to stimuli. Following a total of two to three SGBs, the remission of symptoms has been described to last for several years. Furthermore, the sympathetic deactivation by using SGB has been reported to reduce—or even eliminate—the need or psychotropic pharmaceuticals (Mulvaney & McLean, 2010).

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CASE REPORT/RESULTS OF SGB

This report is a summary from a YouTube video made at Walter Reed Hospital (Mulvaney, 2014). The report is focused on the patient called "Luke," a 35 year-old, Caucasian US Army Ranger.

METHODS

Stellate Ganglion Block

The details of how the SGB was performed on the discussed patient are unavailable. However, since the report is from Walter Reed hospital, conventional protocol likely was used (ultrasound-guided SGB) and can be found in publications from same institution (Mulvaney, 2014).

Psychometric Testing

The PTSD Checklist–Military Version (PCL-M) is a 17-item, one-page, self-report questionnaire, endorsed by the National Center for PTSD, that has strong internal consistency, test–retest reliability, and convergent validity with other PTSD measures. The PCL has been validated for screening for PTSD, for diagnosing PTSD, and for determining response to treatment interventions (Keen & Kutter, 2008). Although there is some debate on what exact score constitutes a positive screen, a score of 35 is generally considered to be the threshold for screening military populations (Keen et al., 2008).

Report of symptoms prior to SGB: Luke reported that, prior to treatment, he was very easy to anger, easy to explode, and had a significant libido reduction that was problematic to the patient, leading him to avoid intimate contact. He also reported severe discomfort being in crowds. Luke reported having failed several conventional treatments for his PTSD, which included a PTSD support group and medications, specifically sertraline hydrochloride (Zoloft) and bupropion hydrochloride (Wellbutrin). He also had been drinking alcohol in an attempt to self-medicate. At the time of presentation for SGB, his PCL-M was noted to be 63. His wife reported unspecified violence again her and property.

The patient underwent an SGB.

Report of symptom improvement 3 months after SGB: The following changes were reported by the patient: His sexual function returned to normal, which he notes to be the change most notable and welcomed after SGB. His out-of-control anger and marital fights resolved, and he had an ability to laugh again and rebuild relationships with his family. *Luke's wife* reported "best 3 months of marriage (3 months following SGB)," and that "I fell back in love with my husband." At the follow-up, Luke's PCL-M was reported to be 32, a marked reduction from the prior-to-SGB score of 63.

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DISCUSSION

Proposed Mechanism of Action for Invasive SNS Procedures on PTSD

The best-understood member of the neurotropic family, nerve growth factor (NGF), regulates a variety of signaling events, such as cell differentiation and survival, growth cessation, and apoptosis (death) of neurons (Snider, 1994). The body responds to chronic stress by increasing NGF levels (Smith, 1996), and NGF is also elevated immediately prior to soldiers' first parachute jump (Alleva & Petruzzi, 1996), thus demonstrating a connection between NGF, stress, and possibly, PTSD. Further studies have demonstrated an increase of intracerebral NGF, leading to retrograde transport of NGF from the intracerebral site to the stellate ganglion (Johnson et al., 1987). Next, an increased concentration of NGF at the stellate ganglion has been shown to lead to sprouting (new nerve growth) at the sympathetic end terminals, which is NGF-dependent (Chen et al., 2001) and, in turn, causes increased NE levels. This cascade has been demonstrated in a rat model, where infusion of NGF in the rat brain leads to an increase in NE (Isaacson & Billieu, 1996). More evidence points to NE being involved in PTSD, in which urine levels of NE are known to increase (Kosten, Mason, Giller, Ostroff, & Harkness, 1987).

Thus, it appears that trauma triggers a neurobiological cascade that ultimately leads to PTSD. Current theory explaining SGB effect on PTSD symptoms is in part based on the observation of that when local anesthetic is applied to the stellate ganglion nerve tissue, a significant reduction of NGF is noted (Takatori & Kuroda, 2006). This decrease in NFG leads to the death of new nerve shoots, a finding demonstrated by Dr Gatzinsky (Gatzinsky & Thrasivoulou, 2004), and, ultimately, a reduction in sprouting. This "pruning" of the sprouts is considered to reduce the density of sympathetic fibers, reducing NE levels and reversing PTSD symptoms.

It is important to recall that while the evidence described here has been reported, the interpretation of the evidence is still considered to be theoretic. Above was originally published in the "Unified theory linking the prolonged efficacy of the stellate ganglion block for treatment of PTSD" (Lipov & Joshi, 2009).

Proposed Mechanism of Action for Invasive SNS Procedures on Sexual Dysfunction Related to PTSD

The CNS has both excitatory and inhibitory systems, which together provide a "dual control" over sexual response and, consequently, sexual behavior (Bancroft, 1999). The limbic system clearly plays a central role in the organization and implementation of sexual behavior. This includes the hypothalamus, amygdala, septum, and ventral striatum (Bancroft, 1999). Sexual behavior, as one of the behaviors organized in the limbic system, requires coordination of endocrine and autonomic responses together with the specific behavior. The focus of this chapter is noradrenergic effects, mainly due to SGB intervention, that is proposed to affect NE.

Interestingly, drugs which increase central NE transmission or availability at alpha receptors increases various aspects of male rat sexual behavior consistent with an enhancing effect on central sexual arousal (Bitran & Hull, 1988). Central effects, however,

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appear to be complex. Sala et al. (1990) demonstrated an inverted-U dose–response curve, with middle doses producing maximal enhancing effects and high doses inhibitory effects (Sala, 1990).

It has been proposed that SGB works by reducing NE levels in the CSF. Jeong et al. (2014) reported significant reduction in EEG activity in a rat model after administration of SGB with 0.2 ml of 0.25% bupivacaine (Jeong & Jeon, 2014). Yeo and Jeon (2015) performed a similar experiment in a placebo-controlled human trial and found that, in the SGB group, bispectral index values (a simplified EEG) significantly decreased after the intervention as *compared to baseline* ($P < 0.05$) (Yeo & Jeon, 2015). The values were also significantly decreased in the SGB *group compared to the values in sham group* after the intervention ($P < 0.05$) (Yeo & Jeon, 2015). Both researcher teams remarked that the reduction in the EEG activity was likely connected to a reduction in intracerebral NE.

Thus, it would be consistent with this view that high concentrations of NE at the extreme right side of the inverted-U will be reduced and that having midrange NE levels would produce maximal sexual-enhancing effect (Figure 3.1).

Finally, objective data from functional magnetic resonance imaging (MRI) and retrograde viral tracing seem to be consistent with neurological structures commonly involved in PTSD as well as sexual function that may be impacted by utilizing SGB. The structure under discussion is the right-sided amygdala, which is chronically activated in patients with PTSD (Liberzon & Martis, 2006). The stellate ganglion has been shown to be connected to the amygdala via second- or third-generation sympathetic neurons (Westerhaus & Loewy, 2001). Recently effect of SGB has been evaluated by the use of positron-emission tomography (PET), which utilizes a positron-emitting radionucleotide to produce computer-constructed, three-dimensional images displaying the function of tissues. In a study by Alkire et al. (2015), PET scans were obtained before and after SGB for PTSD treatment. The

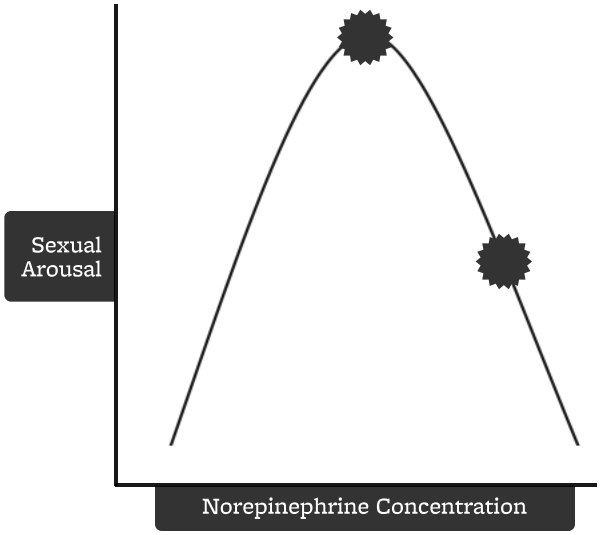


FIGURE 3.1 Relatively low sexual arousal is associated with relatively high concentration of norepinephrine (NE) at point 1, as compared to relatively high sexual arousal with relatively low concentration of NE at point 2.

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results showed that SGB dramatically reduced PTSD symptoms in three of five subjects (60%). Importantly, brain regions that correlated with the individual Clinician-Administered PTSD Scale (CAPS) scores improvement and deactivation of neural structures following SGB centered on the amygdala and hippocampus, primarily in the right hemisphere (Alkire et al., 2015). This is consistent with previous reports of the right amygdala/hippocampal areas being relatively overactive when PTSD symptoms are prominent. As a reference, CAPS is similar to the PCL-M. For the PCL as a whole, the correlation with the CAPS was 0.929, and diagnostic efficiency was 0.900 (Blanchard & Jones-Alexander, 1996).

Interestingly, deactivation of the amygdala was noted following ejaculation (Holstege et al., 2003). Can normal sexual function be a natural antidote to development and/or maintenance of PTSD? Can lack of normal sexual function contribute to persistent PTSD in men? Much is left to be discovered in the association of PTSD and sexual dysfunction. However, sympathetic modulation likely is an important tool to improve sexual function, and SGB may contribute significantly in the treatment of sexual dysfunction associated with PTSD. Of course, further studies are necessary to evaluate sympathetic modulation and SGB as treatment for sexual dysfunction.

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