



PTSD in Women Returning From Combat:
Future Directions in Research and Service Delivery

A Report by the
Society for Women's Health Research

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As of September 30, 2008 over 200,000 women were serving on active duty in the U.S. military,¹ and women make up approximately 14% of deployed forces. While women are technically barred from serving in combat,² they are serving in forward positions in greater numbers. Additionally, as of 2008, there were approximately 38,000 U.S. citizens serving as contractor personnel in Iraq³ – many of whom are women. These new role for women in military operations brings with it physical and mental health concerns, namely posttraumatic stress disorder or PTSD. PTSD affects approximately 2.6% of the U.S. population.⁴ Among military personnel serving in Operation Iraqi Freedom (OIF) and Operation Enduring Freedom (OEF), more than 17% percent of service members surveyed screened positive for PTSD.⁵

Research has shown that there are significant sex differences in diagnosis and treatment of PTSD in the general public.^{4,6} However, much less is known about PTSD in women returning from combat. As the proportion of female veterans is projected to be 14% by the year 2010, it is critical that military, Department of Veterans Affairs (VA), and private sector providers are prepared to identify and care for the unique needs of female service members, veterans, and contractors with PTSD.

To assess the current state of the science, knowledge gaps, and research priorities on the issue, the Society for Women's Health Research* convened an expert workshop on December 8, 2008 in Washington, DC. Attendees discussed what is currently known about PTSD in women returning from combat and developed a roadmap for improving the diagnosis and treatment of PTSD in female service members. The following paper reflects a summary of the day's discussions. It is not meant as a comprehensive review of the literature. A list of frequently used acronyms is available in Appendix I. Additional source information was used to supplement the discussion of the participants. References for these sources are given in the text.

Background – What is PTSD and What Are Its Causes

According the National Institute of Mental Health, PTSD is a condition that develops after a distressing ordeal that involved physical harm or the threat of physical harm. This harm may have happened to the person who develops PTSD or to a friend or loved one or may have simply been witnessed by the person who developed PTSD.^{7,8} People with PTSD may suffer flashbacks to the traumatic event, become aggressive or withdrawn, have nightmares, and become emotionally numb or even violent. Symptoms of PTSD usually appear about three months after the traumatic event. PTSD generally affects twice as many women as men, and women with PTSD report having a lower quality of life than do men with PTSD.⁹ The time to remission of PTSD symptoms is longer in women than in men, and the rate of remission in women is half that

* This workshop was cosponsored by the National Institute of Mental Health, DynCorp International, and Magellan Health Services.

in men.¹⁰ For more information regarding criteria for diagnosing PTSD, please refer to Figure I. For a discussion of the neurobiological pathways of PTSD, please refer to Appendix II.

Figure I. Criteria used for diagnosing PTSD†

Criterion A1: A person is exposed to a life-threatening event either directly or through an experience happening to someone significant to him or her.

Criterion A2: The event results in an intense, overwhelming sense of fear or horror or the person becomes disorganized in their response to the trauma. This reflects a neurobiological response to stress. Men generally have a greater number of A1 events, while women have a greater overall exposure to both A1 exposures and A2 symptoms.

Criterion B: Re-experiencing the traumatic event, characterized by five symptoms: 1) recurrent, intrusive, distressing recollections including thoughts, images, and perceptions; 2) recurrent, distressing dreams; 3) acting or feeling as if the traumatic event were recurring (reliving, illusions, hallucinations, dissociative flashbacks); 4) experiencing psychological distress at exposure to internal or external reminders or cues; and 5) a physiologic reactivity at exposure to cues.

Criterion C: Symptoms of avoidance. These symptoms can manifest as avoiding thoughts, feelings, conversations, people, activities, or places related to the traumatic event. Persons exhibiting avoidance may also experience partial or total memory loss surrounding the traumatic event. The individual may also suffer from diminished interest in important activities or feel detached or estranged from others. They may also have a limited range of affect, meaning they are unable to experience loving feelings. They may also exhibit a foreshortened sense of future, e.g., one doesn't expect to have a career, marriage, or normal lifespan.

Criterion D: Persistent symptoms of increased arousal. These symptoms of arousal (e.g., difficulty falling or staying asleep, irritability or outbursts of anger, difficulty concentrating, hyper-vigilance, and exaggerated startle response) were not present prior to the traumatic event.

Criterion E: The symptoms of criteria A, B, C and D must be present for at least one month.

Criterion F: The above symptoms must result in significant distress or impairment in social, occupational, or other important areas of functioning.

†From the *Diagnostic and statistical manual of mental disorders DSM-IV-TR*, Fourth Edition. American Psychiatric Association; 2000.

What Causes Sex Differences in PTSD?

Workshop participants engaged in a detailed discussion of potential causes of sex differences in PTSD. Participants noted that animal models have shown that male and female rats process stress differently. They also noted that male rats tend to develop more acute reactions (i.e., they can respond quicker) to stressors while females exhibit greater object memory after a traumatic event, meaning they learn to recognize stressors in the future. While these behaviors may pose evolutionary advantages for each sex, in humans they lead to women “holding onto” negative memories more so than men, causing women to “relive” the traumatic event more than their male counterparts. Participants also shared that in general, males also exhibit a faulty memory during times of high stress, possibly protecting them from PTSD. Women react more negatively than men to interpersonal stressors and laboratory stressors. Women also show more ruminative coping. In general women have greater frequency and intensity of negative emotions. Women have more startle modulation and autonomic responses to aversive content – all of which can make women more susceptible to developing PTSD.

Workshop participants also theorized that sex difference in the hypothalamic-pituitary-adrenal (HPA)

axis, a major part of the neuroendocrine system that controls reactions to stress and regulates many body processes, may also contribute to disproportionate rates of PTSD in women and men.

The HPA axis plays a major role in the body's reaction to stress. A study by Uhart *et al.* found that men have a greater HPA axis response to psychological stressors than women while females have greater hormonal reactivity to chemical stressors such as naloxone.¹¹ More research is needed into these sex differences as they relate to the development and treatment of PTSD.

Sex and Gender Issues in Combat-Related PTSD

In considering the diagnosis, prevention, and treatment of PTSD, workshop participants noted that there are unique issues facing female active military personnel, veterans, and other women returning from combat. They are affected by a number of trauma-related conditions, including, but not limited to, PTSD, traumatic grief, unexplained somatic symptoms, depression, sleep disturbances, increased use of tobacco and alcohol, and increased family violence and conflict. A 2004 study found that returning OIF/OEF service members were significantly more likely to suffer from mental health problems, including PTSD, than those not exposed to combat. Of those reporting mental health issues, only 20-40% sought medical care. Perceived barriers to care included fear of stigmatization, lack of trust in the medical system, and lack of knowledge of how to access care.⁵ A study that estimated prevalence in the entire deployed force as of 2007 showed that the number of combat traumas experienced while deployed was the single best predictor of PTSD as well as of major depressive disorder (MDD), and that only half of those with a probable current disorder had sought any mental health treatment in the prior year. Perceived barriers to care included concerns about the effectiveness of treatment as well as institutional barriers such as lack of confidentiality and potential harm to the military career.¹²

Traumatic brain injury is another contributing factor to PTSD in men and women returning from combat. A 2008 study of combat service members found that almost half of service members suffering from mild traumatic brain injuries also met the criteria for PTSD.¹³ Because diagnostic techniques and evidence-based treatment protocols for post-concussive symptoms for combat-related head injuries are lacking,¹⁴ more research is needed into the appropriate diagnosis and treatment of PTSD in service members with traumatic brain injury.

PTSD and Females Military Personnel

Because the female facing combat conditions is a relatively new phenomenon, little is known about the unique needs and issues facing the female service member and other women with combat-related PTSD. Workshop participants discussed a recent, informal survey of health care providers at Walter Reed Army Medical Hospital and Bethesda Naval Hospital that found that approximately 13% of active duty patients with PTSD were women.¹⁵ Of the responding clinicians, 35% stated that their female patients reported more depressive symptoms than did their male patients. Male patients reported more irritability and anger, nightmares, and flashbacks. The responding clinicians also stated female patients are more receptive to psychotherapy while men expressed a stronger preference for medication. An important sex difference in PTSD in combat troops is that almost 65% of the respondents said that sexual trauma (either childhood or in theater) was an issue in the treatment of their female patients with PTSD. No respondents cited sexual trauma as an issue for male patients. For men, the traumatic event was related to killing or seeing people killed or injured.¹⁵ Workshop participants shared that army medical data demonstrate that about 11% of identified cases of PTSD from

OIF/OEF are in females, which is similar to the proportions of women serving in those theaters.

Treatment of Combat-Related PTSD

Of interest to the workshop participants were possible new treatment modalities for PTSD. Discussion centered on the role of allopregnanolone (ALLO), a neurotransmitter that mediates the fear response, in the treatment of PTSD. The same enzyme that makes ALLO also converts testosterone to its inactive form. Studies in military trainees have demonstrated that testosterone levels actually fall during the military's Survival, Evasion, Resistance, and Escape (SERE) training.¹⁶⁻¹⁸ Workshop participants remarked that when testosterone levels fall, ALLO is reduced, resulting in increased stress and aggression. This aggression can be blocked with the use of a class of antidepressants known as selective serotonin reuptake inhibitors (SSRIs), which normalize the brain's ALLO levels. However, for individuals who do not respond to SSRIs, which is at least 50% of women in treatment studies, participants theorized that it is possible that a more effective medication would be ganaxalone, a synthetic form of ALLO, which has been shown to prevent fear conditioning and anxiety.

Progesterone may be another treatment modality for women with PTSD. As stated earlier, progesterone is a precursor of ALLO. Levels of progesterone fluctuate with a woman's menstrual cycle and pregnancy. Higher levels of progesterone in the luteal phase of the menstrual cycle are associated with higher levels of ALLO and a suppression of the HPA and autonomic responses to stress. Workshop participants theorized that women on steroidal birth control might be at a higher risk for developing PTSD as they do not generally experience a luteal phase during their menstrual cycles. Participants agreed that more research is needed into the use of progesterone in the prevention and/or treatment of PTSD.

Dehydroepiandrosterone (DHEA), a precursor of the sex steroids, is another possible avenue of treatment for PTSD. Studies of DHEA in animals have shown DHEA to increase ALLO and decrease cortisol levels.¹⁹ Levels of dehydroepiandrosterone sulfate (DHEAS), the storage form of DHEA, are 50-70% lower in women.²⁰ During the second half of the menstrual cycle, women metabolize DHEA faster than men, possibly resulting in lower levels of DHEA and leaving women more susceptible to PTSD.

Workshop participants also discussed sex differences in the role of catecholamines in memory retention as catecholamines seem to play a larger role in women's memory retention as compared to men. High levels of catecholamines during stress promote the consolidation of emotionally significant memories.²¹ Beta-blockers such as propranolol, which prevent memory reconsolidation, are frequently given to patients who were exposed to traumatic events to prevent the development of PTSD.^{22,23} However, a recent study of OIF/OEF service members returning home with burn injuries found that propranolol did not prevent PTSD in burn patients. But, this study did not take into account any psychological counseling that may have been received or when that counseling may have occurred in relation to the propranolol administration. The authors concluded that the timing of propranolol administration and psychological counseling resulting in memory reactivation needs further investigation.²⁴

Lastly, workshop participants also discussed the potential role of neuropeptide-Y (NPY) in the

treatment of PTSD. At high levels of stress, NPY makes norepinephrine more effective. In men with PTSD, levels of NPY are extremely low. Combat troops exposed to stress have been found to have lower levels of NPY. Normalizing the levels of NPY may improve the resiliency of the brain to the effects of trauma.¹⁶

SSRIs have shown a positive effect in treating non-combat related PTSD.^{25,26} However, in combat-related PTSD, SSRIs were found to be ineffective.²⁷ Workshop participants remarked that existing research on combat-related PTSD has been conducted primarily on men, and more research is needed to gauge the potential efficacy of SSRIs for women with combat-related PTSD. Research is also needed on the effectiveness of non-SSRI antidepressants for combat-related PTSD.

Cognitive processing therapy (CPT), which includes both cognitive and exposure components, is one of the more effective treatments for PTSD.²⁸ CPT focuses not only on anxiety resulting from trauma, but also on a range of emotions including shame, sadness, and anger. Based on the results of a 2007 study published in the *Journal of the American Medical Association*, the VA is currently implementing a program of prolonged exposure therapy (a form of cognitive processing therapy to treat PTSD in female service members). The 2007 found that prolonged exposure therapy was effective in treating PTSD in female veterans and active duty personnel.²⁹

Cognitive processing therapy and exposure-therapy have shown promise in treating both combat and non-combat related PTSD. As the military and VA implement more programs to treat PTSD in female military personnel, resulting data will help to strengthen and refine the existing knowledge base regarding treatment guidelines.

Other Mental Health Issues Unique to Women in Combat Situations

Workshop participants discussed the fact that while all service members face stress when deployed to a combat area, female service members face unique stressors that may impact their mental health. Participants noted that serving in the military and/or as a military contractor is an atypical career path for women. As such, women in the military may experience feelings of isolation and lack of support from colleagues, friends, and family. Women also bear the stress of often being the primary caregiver for family members – not only for their children, but also for their aging parents. The stress of extended deployments for these women is compounded by the demands of caring for their families back home. Participants also remarked that the lack of adequate and safe hygiene facilities for women in combat can lead to both physical and mental health issues. For example, a lack of adequate facilities for urination can lead to an increase in bladder infection. As many latrines are somewhat isolated, women also face a threat (either real or perceived) to their personal safety when faced with the need to urinate. Stressors such as these can contribute to, compound, and/or complicate the diagnosis and treatment of PTSD in women.

Prevention and Treatment of PTSD in Theater

When a service member or contractor is diagnosed with PTSD, is it better for her to be medically discharged or to be treated in theater and returned to duty? Participants noted that when service

members are discharged, they lose the support and structure of steady employment. According to workshop participants, the military has recognized that PTSD and mental health are significant issues for combat troops and has deployed over 200 mental health providers to Iraq. The purpose of these providers is to prevent mental health disorders, as well as to treat and restore affected service members to active duty. In 2006, the Department of Defense issued guidelines for deployment and continued service for military personnel who are suffering from psychiatric disorders or who are prescribed psychiatric medications.³⁰ These guidelines allow for the use of SSRIs and other psychiatric medications in theater when appropriate, but codify the prohibition against the use of other psychiatric medications such as lithium and antipsychotics. The military has also developed web-based programs to help service members cope with the stressors of deployment and combat.^{31,32}

Despite these efforts, the military still faces significant challenges to providing appropriate mental health services to service personnel. Workshop participants identified these challenges as including a growing population of service members suffering from PTSD, a shortage or trained providers, multiple deployments, and traumatic brain injury. Upon being released from active duty, service members access services through the VA or private providers. More research is needed on how to best provide mental health services to both active duty personnel and veterans. There is ongoing research in VA on the provision of mental health services, and also on screening for PTSD. The military has also implemented various programs aimed at better screening. Workshop participants noted that there might be a need to collaborate with the private sector to improve the screening on veterans in the private health care sector.

Workshop participants also noted that consultants and military contractors exposed to combat situations face similar challenges and barriers to obtaining appropriate services to diagnose and treat PTSD. More research is needed to assess what services are available to these women, both in theater and when they return home.

Military Sexual Trauma and PTSD

Aside from trauma directly related to combat experiences, female service members face the risk of military sexual trauma (MST), the term that the Department of Veterans Affairs uses to refer to experiences of sexual assault or severe, repeated sexual harassment experienced during military service. As noted by workshop participants, MST is not a uniquely female problem. While the percentages differ, the absolute numbers for veterans – male and female – who have suffered MST are fairly comparable. Gender responses to MST may differ, and research is ongoing regarding this issue. According to the National Center for PTSD, there is almost no empirical data comparing MST to sexual trauma that occurs outside of military service, although there is anecdotal evidence the MST is unique from and has quantitative and qualitative psychological outcomes.³³

In a 2005 study of Gulf War veterans, Kang *et al.* found that exposure to sexual assault during deployment conferred a greater risk of developing PTSD than did combat exposure.³⁴ In 2002, approximately 3% of active duty military women and 1% active duty military men experienced sexual assault.³⁵ A more recent report found that 6.8% of active duty women and 1.8% of men

reported unwanted sexual contact.³⁶ New screening programs can detect MST and facilitate access to mental health services for both male and female victims of MST, thereby mitigating the burden of psychiatric illness for these service personnel.³⁷ Workshop participants praised the VA for being proactive in addressing MST by mandating universal screening of all veterans for a history of MST. According to workshop participants, each VA facility has identified a Military Sexual Trauma Coordinator to oversee the screening and treatment referral process.

New Systems of Care for Combat-Related PTSD

A study published in 2004 found that for those Iraq war returnees who screened positive for a moderate to severe mental health disorder and wished to receive help for those services, only 23-40% reported receiving professional help in the preceding 12 months.⁵ A more recent survey found that only 53% of military personnel with a probable diagnosis of PTSD had sought care in the previous year. Of those who sought care, just over half received minimally adequate care.¹² In 2007 the military launched RESPECT-Mil (Re-engineering Systems of the Primary Care Treatment (of depression and PTSD) in the Military) to improve access to mental health services for those military personnel suffering from PTSD and depression. The program involves routine screening for PTSD and depression during all primary care visits, assessing all those who screen positive for depression and PTSD, referrals to appropriate treatment, and care coordination and follow-up by primary care providers.³⁸ This program may be particularly effective for identifying and treating PTSD in female service members and veterans since women are more likely than men to report problems to and seek help from their primary care providers.^{39,40} The VA and military are also exploring other avenues of treating PTSD. An internet-based, therapist-assisted self-management program for PTSD has shown promise as a means to deliver effective treatment to service personnel.⁴¹

The VA system will be an invaluable source of mental health services for women returning from deployment. Currently, 12%, or more than 45,000, of the total number of OEF/OIF veterans using VA services are women. Workshop participants noted that female veterans may be more likely to use VA care than are their male counterparts, but that women may be less likely than men to report PTSD symptoms in a VA setting. Participants noted that women are more likely to report depression and general anxiety symptoms and are twice as likely to be diagnosed with personality disorders. Workshop participants praised the VA for being a leader in its efforts to care for the female veteran, citing the VA's appointment of a full-time Women Veterans Program Manager at every VA facility and a Women's Health Science Division in the National Center for PTSD as examples of its leadership. They also discussed the need for the VA to develop more gender-sensitive programs for diagnosing and treating PTSD in female veterans.

Diagnosing and Treating Combat-Related PTSD in the Private Sector

Once a female service member becomes a veteran or a contractor/consultant returns home, new problems accessing services for PTSD can arise. Since PTSD symptoms do not generally manifest until three to six months after a traumatic event,⁷ many women may leave the military without a diagnosis of PTSD in their medical charts. Workshop participants stated that upon leaving active duty, many women, especially those who were/are reservists, may receive their

healthcare through the private sector. Participants noted that veteran status is not generally ascertained in most health plan and employer eligibility files. Without an adequate history of veteran status, providers may not screen for combat-related disorders. Further complicating the delivery of services for women is that even if the provider knows a patient's veteran status, there is a misperception about women's roles in the military – that women are not directly exposed to combat situations. As such, PTSD symptoms may go unrecognized or be misdiagnosed. Private sector providers not familiar with the treatment of PTSD may mistakenly prescribe drugs such as benzodiazepines for symptom management, despite the fact that benzodiazepines have not been shown to be effective in treating PTSD.⁴² Workshop participants cited a concern that when private sector physicians do recognize PTSD symptoms in their patients, they may not be familiar with the VA and available services for PTSD. Further, there is a financial disincentive to the physician for referring patients to the VA for care.

Participants discussed the opportunities for the private sector to improve the diagnosis and treatment of combat-related PTSD. For example, during this workshop, Magellan Health Systems presented information about its CME programs promoting evidence-based practices guidelines for diagnosing and treating PTSD. These training programs include modules on military cultural competence and meeting the mental health needs of returning veterans.⁴³ Further research is needed into developing appropriate screening and treatment of PTSD for service members returning from combat and reentering into the private sector.

Summary: Developing a Research Agenda and Improving Patient Care: What Health Care Professionals Need to Know

As the above report states, there are multiple areas in which our knowledge of PTSD in female service personnel is lacking. Most research models for PTSD were built around men. These models will need to be reexamined and redesigned to better target women. In the field of psychobiology, there is a need to look for new models for high stress populations in which there are a greater proportion of women (e.g., competitive athletes, law enforcement personnel) as an approach to supplement our limited knowledge of sex differences in the development of PTSD. Additionally, while research has been examining the role of sex hormones (estrogen in women and testosterone in men) in the development of PTSD, researchers should also look at the effects of androgens in women and estrogen in men.

Genetics may also play a significant role in the development of PTSD. More research is needed into the effects of polymorphisms in ethnic groups, as well as the effects of polymorphism on the effectiveness of medications and cognitive approaches to treating PTSD. In order to facilitate genetic studies, the Department of Defense and the VA will need to coordinate efforts and facilitate the implementation of research networks across facilities.

The military furthers our knowledge about combat-related PTSD in women by developing command awareness of the importance of medical studies to promote participation by their troops. Recruitment into research studies will be especially important for women as this will be the first time we will be observing the effects of combat on a large number of female service members. As the military begins to draw down from its current theaters of combat and women are released from active duty, it is important that we track how they are discharged and with

what medical appointments or treatment referrals.

As women are returning from combat to their families, we will need to examine the effects of women's PTSD on families. Additionally, women are at high risk for divorce and domestic violence when men return from combat. Will we be seeing the same for men who have stayed home while their spouses were deployed? Questions to ask include the following:

- How do women react when they return post-deployment?
- How do they treat their spouses, and/or children?
- How do we instill health promotion behaviors early in the separation process and not wait until post-deployment?
- What are the effects of PTSD on parenting and children's mental health?

Researchers need a better understanding of the natural course of PTSD over the lifecourse. Further, we know little about the effect of multiple deployments on women over time. For example, we know that former military men with PTSD are at higher risk for substance abuse. We do not yet know if women develop co-morbid substance abuse problems at the same rate as their male counterparts. A focus on sex differences in treatment and outcomes measurements is needed to better understand the needs of female service personnel.

Ideally we would like to prevent PTSD in our combat troops. Until effective prevention strategies are developed, the best the military can do is to train healthcare professionals in identifying early symptoms of PTSD so that those displaying such symptoms can receive early intervention. As cumulative trauma can significantly increase one's risk for developing PTSD, military healthcare providers will need to be especially cognizant of service members' prior exposure to combat and other stressors, whether through multiple deployments or service members' experiences prior to enlistment.

Within the military system, military leaders should talk to their troops about the importance of seeking help for mental health disorders. The language and attitudes of commanders can significantly impact a service member's willingness to seek and comply with mental health treatment. Service members need to be able to believe that getting mental health care won't impact their career.

In the private sector, clinicians first and foremost need to know a woman's military status. As stated earlier, clinicians in the private sector do not routinely screen for military service. Training must be provided to primary care physicians including OB/GYNs, to help them identify potential cases of PTSD in their female patients and to assist them in making informed referrals for these patients. Possible avenues for such training programs include health plans and medical professional societies. Additionally, models for collaboration between private sector and VA providers need to be developed to overcome private sector physicians' fear of 'losing' patients to the VA system.

Private sector clinicians need more and better tools for opening a dialog about PTSD with their female patients. Posters about the signs and symptoms of PTSD could be posted in waiting

rooms or restrooms of clinics. These posters could trigger a discussion of symptoms between patient and provider. Clinicians need better and more appropriate screening tools, as well as access to suitable resources if a patient does screen positive for PTSD.

All clinicians need to have a better understanding of the role of co-morbidities as they relate to PTSD. In the absence of better screening tools for PTSD, co-morbidities such as alcohol and substance abuse, irritable bowel syndrome, and migraines may signal an underlying case of PTSD. We need to develop effective working relationships across systems at the state, federal, and local, as well as across the military and private sector. A better electronic infrastructure is essential for sharing medical records across these systems. The Departments of Defense and Veterans Affairs, as well as the private sector, have been working on such systems for some time. Attention should now be focused on making those systems work across agencies and public/private sectors.

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APPENDIX I: LIST OF ACRONYMS

ALLO	Allopregnanolone
CPT	Cognitive Processing Therapy
DHEA	Dehydroepiandrosterone
DHEAS	dehydroepiandrosterone sulfate
HPA	Hypothalamic-Pituitary-Adrenal
MDD	Major Depressive Disorder
MST	Military Sexual Trauma
NPY	Neuropeptide-Y
OIF	Operation Iraqi Freedom
OEF	Operation Enduring Freedom
PTSD	Posttraumatic Stress Disorder
SERE	Survival, Evasion, Resistance, and Escape (SERE) training
SSRI	Selective Serotonin Reuptake Inhibitors
VA	Department of Veterans Affairs

APPENDIX II: The Neurobiological Pathways of PTSD

Workshop participants shared the following information about the neurobiology pathways involved in the development of PTSD. For a more complete discussion regarding the neurobiology of fear, please refer to The Neurobiology of Mental Illness, Dennis Chamey and Eric Nestler, eds.⁴⁴

When one is under threat, fear signals are sent through the thalamus, stimulating the hypothalamic-pituitary-adrenal (HPA) axis, a major part of the neuroendocrine system that controls reactions to stress and regulates many body processes, including digestion, the immune system, mood and emotions, sexuality, and energy storage and expenditure. The fear response is further mediated by the neurotransmitters GABA_A and allopregnanolone (ALLO). Normally, there is a “brake” on this system, however, with fear conditioning, the GABA/ALLO receptors are dismantled.

Also involved in this process is the amygdala. The amygdala is a primitive, all-or-none response organ located near the brain’s hippocampus, in the frontal portion of the temporal lobe. Among its functions is to interpret a stimulus as being a threat. The frontal lobe of the brain then finely discriminates arousal signals and inhibits the amygdala when appropriate.

A certain level of arousal is beneficial. To a certain point, people think better when aroused. However, at high levels of arousal, neurotransmitters engage alpha 1 receptors and the amygdala takes over. The HPA axis then sends out a cocktail of neurotransmitters including cortisol, ALLO, neuropeptide Y (NPY), and DHEA to regulate the strength of the fear response.

There are interesting sex differences in regards to ALLO that may pertain to the treatment of PTSD. One study found that ALLO is 40% lower in women with PTSD.⁴⁵ Since progesterone, a precursor of ALLO, was high in these women, it suggests that these women have a block in the conversion of progesterone to ALLO.

PTSD and Depression

PTSD and depression are highly co-morbid, with 50% of PTSD patients experiencing depression. Major depressive disorder (MDD) after a trauma is associated with PTSD in more than 90% of cases, meaning that depression after a trauma rarely occurs in the absence of PTSD. Co-morbid depression and PTSD are difficult to treat. Studies have shown that ALLO levels are lowest in PTSD patients with co-morbid depression. Cortisol output is also increased in women with PTSD/MDD. Early studies in women suggest that the ALLO/DHEA ratio is lower in women with PTSD/MDD, possibly making them more resistant to treatment.⁴⁵