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Peptide Signaling and Whole-Person Health in Veterans with Chronic Stress and Trauma-Related Symptoms: A Narrative Literature Review

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Abstract: Veterans experiencing chronic stress or trauma-related symptoms may experience sleep disturbance, altered stress regulation, inflammation, pain, and reduced quality of life. This narrative literature review examines peptide signaling as a possible biological framework for investigating interconnected regulatory processes within a whole-person approach to veteran health. It distinguishes endogenous peptide signaling from research on administered peptide compounds and organizes the literature into direct veteran evidence, general stress physiology evidence, and peptide science evidence. Neuroendocrine and neuroimmune communication provide plausible research connections, but mechanistic findings cannot establish clinical effectiveness. Semax and Selank are considered illustrative mechanistic examples, not established interventions. Wound healing is addressed only as a secondary, exploratory dimension of tissue repair. The literature supports investigating peptide-related signaling questions in conjunction with veteran-centered functional and patient-reported outcomes; it does not establish that peptide compounds improve veteran health. Future studies should use population-specific designs, distinguish biological mechanisms from interventions, and communicate uncertainty clearly.

Keywords: Veterans, Peptide Signaling, Chronic Stress, Neuroendocrine Regulation, Whole-Person Health

Introduction

Veterans experiencing chronic stress or trauma-related symptoms may present with concerns that extend beyond psychological distress. The National Center for PTSD (n.d.) reported that 7% of veterans experience PTSD at some point in life, while 15% of Operations Iraqi Freedom and Enduring Freedom veterans experienced PTSD in the past year and 29% experienced PTSD at some point in life. PTSD and chronic stress have also been associated with neurobiological, sleep-related, immune, endocrine, pain-related, and quality-of-life concerns (Pitman et al., 2012; Schnurr et al., 2009; Yehuda et al., 2015). These findings support a whole-person review that examines regulation and recovery across interacting systems rather than focusing only on diagnosis.

Integrative health provides a useful framework because it emphasizes coordinated care and the whole person. The National Center for Complementary and Integrative Health (NCCIH, 2021) described integrative health as the coordinated use of conventional and complementary approaches with attention to whole-person care. The National Academies of Sciences, Engineering, and Medicine (2023) similarly described Whole Health as an approach that considers biological, behavioral, social, and environmental domains of well-being. This framework matters because veterans may experience stress-related symptoms in the context of sleep, pain, family life, meaning, physical function, and overall quality of life.

In this review, integrative peptide science refers to the study of peptide signaling and peptide-related mechanisms as they may relate to biological regulation, stress physiology, inflammation, and whole-person wellness. The term is used descriptively rather than as an established clinical specialty. Endogenous peptide signaling concerns peptides produced within the body and their roles in physiological communication; research on administered peptide compounds asks a different question—whether an external intervention is safe and effective for a defined population and outcome. Evidence of a signaling mechanism cannot by itself justify a treatment claim (Fosgerau & Hoffmann, 2015; Muttenthaler et al., 2021). This distinction is especially important for veterans because findings from biochemical assays or animal models cannot be assumed to predict clinical benefit in people with trauma-related symptoms.

Problem Statement

The anchor for this problem is that veterans with chronic stress or trauma-related symptoms may experience measurable concerns across psychological, sleep, inflammatory, neuroendocrine, pain, tissue repair, functional, and quality-of-life domains. The hook is that PTSD is slightly more common among veterans than civilians, with 7% of veterans experiencing PTSD at some point in life and higher rates among OIF/OEF veterans (National Center for PTSD, n.d.). These data make the problem observable and relevant to veteran health.

The general problem is that veterans experiencing chronic stress or trauma-related symptoms may experience interconnected disturbances in sleep, neuroendocrine and immune regulation, pain, functioning, and quality of life. The specific conceptual gap is that these concerns are often considered separately, while the contribution and limitations of peptide signaling as a research lens are not always distinguished from claims about peptide-based interventions. This review therefore separates direct veteran evidence, general stress physiology evidence, and mechanistic peptide science evidence. Wound healing is considered only as a limited, exploratory example of tissue repair rather than a demonstrated veteran outcome.

Purpose Statement

The purpose of this narrative literature review is to examine whether endogenous peptide signaling offers a useful biological framework for interpreting neuroendocrine and immune communication in the context of chronic stress and trauma-related symptoms among veterans. The review synthesizes relevant veteran, general physiology, and peptide research; distinguishes biological mechanisms from administered peptide interventions; and considers wound healing as a secondary exploratory topic. Its purpose is to identify research questions and evidentiary limits, not to establish peptide compounds as treatments for veterans.

Research Question

What does the literature suggest about endogenous peptide signaling as a conceptual framework for investigating neuroendocrine and immune regulation, and their relationship to whole-person health outcomes, among veterans experiencing chronic stress or trauma-related symptoms?

Search Strategy

Literature was located through PubMed, Google Scholar, PsycINFO, CINAHL, MEDLINE, ProQuest, ScienceDirect, and Saybrook University library resources. Search terms included veterans, PTSD, chronic stress, trauma-related symptoms, sleep quality, quality of life, inflammation, neuroendocrine regulation, allostatic load, peptide signaling, peptide therapeutics, Semax, Selank, BDNF, tissue repair, wound healing, integrative health, Whole Health, and whole-person wellness. Boolean phrases included “veterans” AND “PTSD”

AND “inflammation,” “PTSD” AND “neuroendocrine regulation,” “allostatic load” AND “stress,” “peptide signaling” AND “inflammation,” “peptide therapeutics” AND “neuroendocrine,” “Semax” AND “BDNF,” “Selank” AND “regulatory peptides,” “wound healing” AND “peptide signaling,” and “Whole Health” AND “veterans.”

Sources were included if they were peer-reviewed, written in English, and related to veterans, PTSD, chronic stress, sleep, inflammation, neuroendocrine regulation, peptide signaling, peptide therapeutics, tissue repair, integrative health, or whole-person wellness. Government and institutional sources were included when they provided authoritative definitions or population-level data. Sources were excluded if they were non-scholarly opinion pieces, primarily promotional, unrelated to the research question, or made clinical claims without evidence. Sources published from 2015 to 2026 were prioritized, while older sources were retained when they were foundational theories, landmark models, or early mechanistic peptide studies.

This review separates the evidence into three categories. Direct veteran evidence includes PTSD, sleep, inflammation, quality-of-life, and Whole Health literature involving veterans. General stress physiology evidence includes allostatic load, neuroendocrine regulation, immune signaling, inflammation, and sleep research. Peptide science evidence includes peptide therapeutics, regulatory peptides, Semax, Selank, and mechanistic peptide signaling. This separation is important because indirect or preclinical peptide evidence should not be interpreted as proof of veteran-specific clinical effectiveness.

Theoretical Framework

The biopsychosocial model, allostatic load theory, and salutogenesis guide this review. Engel (1977) argued that health should be understood through biological, psychological, and social dimensions rather than through a narrow biomedical model alone. This theory is relevant because veterans with chronic stress may experience changes in mood, sleep, immune activity, endocrine function, pain, relationships, and meaning. The biopsychosocial model supports a paper that examines peptide signaling within a larger whole-person framework.

Allostatic load theory explains how repeated stress activation may produce cumulative biological burden across systems (Juster et al., 2010; McEwen, 1998). This theory supports the review's focus on neuroendocrine regulation, inflammation, sleep, and recovery as connected systems. Salutogenesis adds a health-promotion perspective by emphasizing factors that support resilience and restoration rather than only disease (Antonovsky, 1996). Together, these frameworks position peptide signaling as one possible biological lens within a broader Whole Health model.

Review of the Literature

Veterans, Chronic Stress, PTSD, and Quality of Life

Direct veteran evidence indicates that trauma-related symptoms may affect more than mental health alone. PTSD is associated with biological stress regulation, sleep disturbance, functional impairment, and quality-of-life concerns (Pitman et al., 2012; Schnurr et al., 2009; Yehuda et al., 2015). Sleep disturbance is especially important because it is a common PTSD-related concern and may interact with immune and inflammatory regulation (Germain, 2013; Irwin & Opp, 2017). This theme supports the research question by showing why neuroendocrine regulation, inflammation, tissue repair, and quality of life are relevant to veterans experiencing chronic stress.

Neuroendocrine Regulation, Inflammation, and Sleep

General stress physiology evidence suggests that chronic stress can influence neuroendocrine and immune communication. Allostatic load theory explains how repeated stress activation may create cumulative physiological burden (Juster et al., 2010; McEwen, 1998). Inflammation has also been studied in PTSD. Passos et al. (2015) reviewed inflammatory

markers in PTSD, Speer et al. (2018) reviewed systemic low-grade inflammation, and Wang et al. (2017) discussed PTSD through an immunological lens. These sources suggest that trauma-related symptoms may involve measurable biological processes, although findings remain complex and should not be oversimplified.

Inflammation, sleep, and mood interact across systems. Dantzer et al. (2008) described immune-to-brain communication in sickness behavior and depression, Slavich and Irwin (2014) examined pathways linking social stress and inflammatory activity, and Irwin and Opp (2017) reviewed reciprocal interactions between sleep and innate immunity. These findings support two specific questions for peptide-focused research: how peptide-mediated neuroendocrine communication relates to prolonged stress responses, and how peptide-related immune signaling might be studied alongside inflammation and sleep. The cited studies establish the relevance of these regulatory domains, not that any particular administered peptide improves outcomes in veterans. Within a Whole Health model, the value of this lens is to identify potentially measurable communication processes while keeping symptoms, function, and lived experience central.

Peptide Signaling, Regulatory Peptides, and Tissue Repair

Peptide therapeutics constitute an established area of biomedical investigation, but the development of peptide drugs must be distinguished from research on endogenous signaling (Fosgerau & Hoffmann, 2015; Lau & Dunn, 2018; Muttenthaler et al., 2021). The peptide-specific contribution of this review is to frame neuroendocrine and neuroimmune communication as candidate processes for investigation across stress, inflammation, and sleep—not to infer a therapeutic effect. Semax and Selank are included as illustrative examples of the distance between mechanistic observation and clinical inference. Kost et al. (2001) examined inhibition of enkephalin-degrading enzymes in human serum, while Dolotov et al. (2006) investigated Semax-associated BDNF and TrkB expression in rat hippocampus. These older biochemical and animal findings illustrate testable pathways, but neither study demonstrates benefit in veterans, establishes a clinically meaningful outcome, or supports a treatment recommendation. Their role here is explanatory rather than evidentiary support for veteran-specific efficacy.

Tissue repair is used narrowly in this review to mean wound healing, including inflammation, cellular proliferation, extracellular matrix formation, and remodeling. Guo and DiPietro (2010) reviewed factors influencing these processes in the broader wound-healing literature. This background is relevant to questions about cellular communication and physical recovery, but it is not direct evidence that chronic trauma-related symptoms impair wound healing in veterans or that administered peptides improve wound outcomes in that population. Accordingly, wound healing is a secondary exploratory research direction rather than a central outcome supported by the reviewed veteran literature. Any future study addressing this question would need a defined wound type, a clinically appropriate population, and prespecified outcomes such as healing time or wound closure, rather than an undefined category of "tissue repair indicators."

Whole Health and Integrative Care for Veterans

Whole Health and integrative care models help prevent this paper from becoming too narrowly biomedical. NCCIH (2021) emphasized coordinated whole-person care, and the National Academies of Sciences, Engineering, and Medicine (2023) described Whole Health as a broader approach to health and well-being. Within the Veterans Health Administration, Whole Health has been described as a shift from asking only what is wrong to asking what matters to the person (Kligler et al., 2022). This model is relevant because veterans may need support that addresses stress regulation, pain, sleep, relationships, meaning, and functional goals.

Mind-body and complementary approaches in veteran populations demonstrate how integrative research can be conducted while still requiring evidence. Polusny et al. (2015) studied mindfulness-based stress reduction for veterans with PTSD, and Hilton et al. (2017) reviewed meditation for posttraumatic stress. These sources do not support peptide treatment claims. Instead, they show that veteran-focused integrative research should remain evidence-based, population-specific, and ethically cautious. Peptide signaling should be held to the same standard.

Research Gaps, Ethical Cautions, and Synthesis

The three evidence categories support different levels of inference. Direct veteran research establishes the importance of trauma-related symptoms, sleep, function, quality of life, and Whole Health; general physiology research describes interacting neuroendocrine, inflammatory, and sleep processes; and peptide research provides mechanistic examples and a distinct field of therapeutic development. Their convergence supports asking whether endogenous peptide-related pathways help characterize stress-associated regulatory patterns, but not concluding that peptide administration improves veteran outcomes. Semax and Selank illustrate mechanistic questions without bridging that clinical evidence gap. Wound healing remains a secondary exploratory topic grounded in broader physiological literature rather than demonstrated veteran-specific effects.

The synthesis therefore yields a specific conceptual contribution: peptide signaling offers a way to formulate and test questions about communication between stress-response and immune systems within a biopsychosocial and Whole Health model. This lens is potentially useful only when investigators distinguish endogenous signaling from administered interventions and evaluate biological observations alongside meaningful outcomes such as sleep, pain, function, and quality of life. The reviewed evidence does not establish peptide compounds as effective clinical interventions for veterans.

Recommendations From the Literature

Use Whole-Person Models in Veteran Wellness Research

Researchers and clinicians should use whole-person models when discussing veteran wellness. The biopsychosocial model, salutogenesis, and Whole Health framework all support attention to biological, psychological, social, functional, and meaning-based dimensions of health (Antonovsky, 1996; Engel, 1977; National Academies of Sciences, Engineering, and Medicine, 2023). This recommendation matters because veterans with chronic stress may require support that addresses sleep, pain, activity, purpose, relationships, and clinical care together.

Separate Peptide Mechanisms From Treatment Claims

Researchers should separate peptide signaling mechanisms from peptide treatment claims. Studies may discuss how peptides participate in biological communication, but they should not claim that peptide compounds improve veteran outcomes unless direct clinical evidence supports that claim. This recommendation addresses the ethical risk of overstating emerging evidence, especially for veterans who may be vulnerable to unsupported wellness claims.

Prioritize Veteran-Specific Research With Biomarkers and Patient-Reported Outcomes

Future research should prioritize veteran-specific designs before making intervention claims. Studies of endogenous signaling could examine clearly defined neuroendocrine or inflammatory measures alongside sleep quality, pain, functional status, PTSD symptoms, and patient-reported quality of life. If wound healing is investigated, it should be a separately justified exploratory outcome with specified wound characteristics and measures such as wound closure or healing time. Biomarker associations alone should not be treated as evidence of clinical improvement, and trials of administered compounds would require independent safety and efficacy evaluation.

Use Interdisciplinary Teams and Clear Ethical Communication

Research on peptide signaling, stress physiology, and veteran wellness should involve interdisciplinary teams with expertise in psychology, neuroscience, immunology, endocrinology, sleep science, rehabilitation, ethics, and integrative health. Ethical communication should clearly state what is known, what is uncertain, and what has not been proven. This approach protects veterans from unsupported claims while still allowing legitimate research on peptide signaling to continue.

Limitations

This narrative review is not a systematic review and may omit relevant studies. The included evidence spans veteran-specific clinical observations, general stress physiology, and older mechanistic or preclinical peptide research, which are not interchangeable levels of support. The reviewed Semax and Selank studies do not establish veteran-specific outcomes, and the wound-healing literature offers only general background for an exploratory research question. "Integrative peptide science" is used as a descriptive conceptual phrase, not a recognized clinical category. These limitations preclude therapeutic recommendations or claims of clinical benefit for peptide compounds in veterans.

Conclusion

This narrative literature review examined endogenous peptide signaling as a possible framework for investigating neuroendocrine and immune communication in veterans experiencing chronic stress or trauma-related symptoms. Its specific contribution is to identify testable questions about regulatory signaling within a broader biopsychosocial and Whole Health model while distinguishing those questions from claims about administered peptide interventions. Semax and Selank illustrate the limits of mechanistic inference, and wound healing remains a narrowly defined exploratory topic rather than a demonstrated veteran outcome. The current literature does not support peptide-based clinical claims for veterans. Future research should combine carefully selected biological measures with veteran-specific clinical, functional, and patient-reported outcomes.

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