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THE LINK BETWEEN TRAUMA, CHRONIC PAIN, AND DISEASE

Jessica Caniff
Eastern Kentucky University, jessicamventura@gmail.com

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BY

JESSICA VENTURA CANIFF

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JESSICA VENTURA CANIFF

Submitted to the Faculty of the Graduate School of
Eastern Kentucky University
in partial fulfillment of the requirements for the degree of

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Dedication

Dedicated to my husband, Jimmy, my daughter, Nola, my son, Wyatt, and my mother, Vicki. You have all made great sacrifices to support me on this long journey. Your unceasing love and support make me whole. I am immeasurably grateful to have you in my life and always by my side.

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ABSTRACT

Psychological trauma and early life adversity have been significantly connected to elevated incidence of disease, chronic pain, and premature death. Trauma exposure can result in shortened telomere length in chromosomes and advanced biological aging. Epigenetics and the modification of gene expression through methylation of DNA can be directly affected by traumatic experiences. Aversive childhood experiences are globally linked to increased likelihood of risk factors for disease, death, and wellbeing throughout life. Sleep deprivation and disruption is a common symptom of trauma exposure and posttraumatic stress disorder. Loss of sleep has a remarkably detrimental impact on the immune and cardiovascular systems and can lead to alterations in DNA. There is a highly graded relationship between psychological trauma and physical illness. Interdisciplinary care has been utilized to address the link between physical and mental illness from a whole health approach. However, more efforts are needed on all fronts in destigmatizing mental illness and gaining a greater understanding of the mind-body connection.

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Introduction

Statement of the Problem and Significance of the Issue

Posttraumatic stress disorder commonly co-occurs with chronic pain and disease, however, the link between these conditions often remains unnoticed in many clinically based settings. Shared characteristics among trauma, chronic pain and disease include anxiety, depression, hyperarousal, behavioral avoidance, emotional lability, and attentional bias to somatic cues (Asmundson et al., 2002). Globally, early life adversity and psychological trauma have been causally linked to conditions of chronic pain and disease.

In his book *The Body Keeps the Score*, author Bessel van der Kolk (2015), described the body's response to trauma as follows: "Bodies register the threat…the mind learn[s] to ignore the messages from the emotional brain, the alarm signals don't stop…stress hormones keep sending signals…Physical effects on the organs go on unabated until they demand notice when they are expressed as illness." Psychological trauma can alter the brain and central nervous system to modify signaling. Chronic pain, disease, and mental illness are common conditions resultant of this sequelae.

Purpose

The primary purpose of this project is to review existing literature on chronic pain, disease, and trauma, and how they are interconnected as well as how they are impacted and exacerbated by coexisting together. Increasing evidence supports a significant connection between life stress and adversity with an elevated incidence of disease and chronic pain in later life. This review aims to shed further light on the comorbidity between mental and physical disorders and will present data on the comorbidity between significant physical ailments and

psychological trauma exposure in order to highlight the broadness of the mind-body connection. Further goals of this review are to provide an extensive dataset that can be utilized to inform clinicians across multiple domains of treatment including medical, psychological, and psychiatric approaches to care. In doing so, a primary objective is that this literature review will contribute to more trauma informed, well-balanced care for those who endure psychological trauma, chronic pain, and disease across the lifespan.

Literature Review

Method of Literature Search

Research was conducted by searching through online academic search engines that included: PsycInfo, EBSCO Host, and Google Scholar. Journals searched included: The Canadian Journal of Psychiatry, Arthritis Care and Research, Psychological Trauma: Theory, Research, Practice, and Policy, Journal of Trauma and Dissociation, The Clinical Journal of Pain, Military Medicine, Annual Review of Clinical Psychology, Journal of Musculoskeletal Pain, Frontiers in Psychology, European Journal of Psychotraumatology, Journal of Affective Disorders, Journal of Psychosomatic Research, Psychoneuroendocrinology, Annals of Behavior Medicine, Primary Psychiatry, Clinical Psychology Review, Health Psychology, International Journal of Psychiatry in Clinical Practice, BMC Psychiatry, Psychosomatic Medicine, Psychology and Psychotherapy: Theory, Research, and Practice, Nature Reviews Neuroscience, Biological Psychiatry, Journal of Traumatic Stress, Psychiatry Research, Clinical Psychology Review, and JAMA Pediatrics. Books searched included: Violence and Trauma in the Lives of Children, Overview of Exposure, and The Body Keeps The Score. Key words searched included: trauma, pain, chronic pain, sleep, sleep deprivation, illness, stress, and telomeres. No restriction was set for timeframe of journal articles or books during the search.

Literature Review

Stress and trauma can alter biology, shorten telomeres, and change DNA.

Telomeres, compound structures at the end of chromosomes, play a pivotal role in aging and display relationships to lifetime adversity, particularly in childhood (Epel & Prather, 2018). Telomere length serves as a biomarker of biological aging and stress. Abuse, neglect, socioeconomic status, and other adverse experiences early in life have been repeatedly associated with poor physical and mental health outcomes (Ridout et al., 2017). In an effort to gain greater insight into the biologic mechanisms underlying these associations, researchers have calculated the relationship between early adversity and telomere length. Telomere length is a marker of cellular senescence, a process of a cell's deterioration with age as a reflection of its inability to divide and grow. Early adversity is identified as having long-lasting physiological outcomes contributing to disease risk and biological aging. Ridout et al., (2017) noted individuals with a significant history of early adversity are at accelerated risk of developing poor physical and mental health outcomes, including diabetes, asthma, depression, anxiety, and posttraumatic stress disorders. Analysis of the biologic mechanisms by which early life adversity elevates risk for poor health outcomes reveals evidence of expedited biologic aging through shortened telomere length. Ridout et al., (2017) further described that when telomeres become critically short, cells may enter apoptosis, a process of programmed cell death. Telomere length has been directly linked to stress responses including inflammation. Many chronic illnesses consist of prolonged states of hypothalamic-pituitary-adrenal axis (HPA) stress and/or inflammation, which may be linked to relations between telomere length and somatic conditions, including heart disease, diabetes, asthma, obesity, chronic pain, irritable bowel syndrome, and neurodegenerative disorders. Proposed mechanisms underlying associations between stress and telomere length

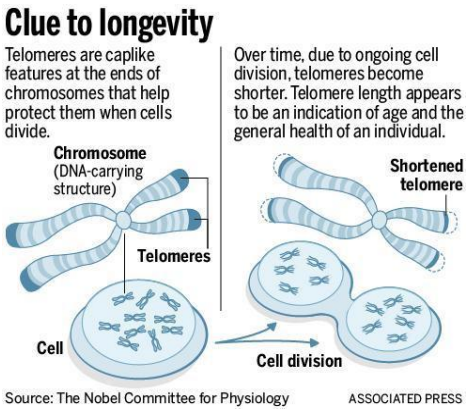
include mitochondrial dysfunction and telomerase inactivation due to heightened and prolonged stress signaling. Ridout et al., (2017) wrote "In addition to reflecting biologic stress, telomere attrition often precedes chronic disease development, suggesting that telomere erosion may be a causal link connecting early adversity and later disease." Some evidence has indicated telomere attrition early in life may be particularly detrimental and result in premature development of stress-related health disorders. Telomere shortening has been associated with adversity at different stages of development and after multiple types of adverse exposures. Further, some analyses have indicated a cumulative and dose-dependent negative relationship between early adversity and telomere length. Early adversity has been surmised to directly activate or be associated with increased cellular stress and replication, which may consequently lead to accelerated telomere shortening. Telomerase activity, a key regulator of telomere length, has been shown to decrease with adversity exposure (Ridout et al., 2017). Telomere repair and lengthening strategies vary depending on the developmental phase of cells. Research cited by Ridout and colleagues indicate telomere shortening may be a mechanism by which early adversity impacts disease risk. The findings may have reflected underlying biological processes initiated by early life adversity, such as dysregulated stress signaling, altered metabolism, and increased inflammation and oxidative stress (Ridout et al., 2017). Adversity early in life not only influences children at an immediate, emotional and physical level, but has also been linked to long-lasting biologically based health sequelae. Of note, meta-analyses have revealed a negative relationship between psychiatric disorders and telomere length, further supporting the link between trauma, chronic pain, and disease (Ridout et al., 2017).

Analyses have found reliable associations between psychopathology and shortened telomere length. Significant evidence indicates impaired telomere biology as a contributing

factor or result of psychopathology. Further studies imply a triadic relationship among stress levels, telomere length shortening, and psychiatric disorders (Epel & Prather, 2018). Chronic psychosocial stress and telomere length were found to have an inverse relationship. Longitudinal data support telomere attrition across stress levels (Meier et al., 2019), which supports the current stress-diathesis model of illness. Cumulative childhood trauma is associated with higher rates of adult psychiatric disorders and poorer functional outcomes (Copeland, 2018).

Figure 1.

Image of Telomere



Early experiences of threat are associated with increased rates of biological aging in children and adolescents (Sumner et al., 2019). Evidence for accelerated development is derived from studies of chromosome telomere shortening or advanced pubertal development. Early threat-related experiences are particularly associated with accelerated biological aging in youths, which is a possible mechanism that links early life adversity with symptoms such as depression (Sumner et al., 2019).

Kalin (2020) cited data that illustrated "the intergenerational transfer of the consequences of trauma through researching the relation between a mother's history of childhood adverse

experiences with telomere shortening and the infant's mental health." Indeed, studies have revealed a relation of adversity occurring during the mother's childhood to her infant's telomere biology. As Kalin (2020) noted that telomeres are housed at the end of chromosomes and operate to defend against chromosomal damage. The reduced physical length of telomeres has been linked to the aging process as well as physical and mental health. Data showing increased levels of adversity in mothers during childhood has been connected to heightened levels of externalizing issues and decreased length of telomeres in their offspring. Previous data has also indicated an interaction between maternal childhood adversity and telomere length on the outcome of externalizing issues (Kalin, 2020).

Epigenetics, the modification of gene expression through DNA, has been frequently referenced throughout recent literature as being directly affected by traumatic experiences. DNA modifications that do not alter DNA sequence can impact gene activity (Reference, 2020). Epigenetic changes result when chemical compounds (such as methyl groups) are added to single genes and the modifications regulate their activity. These modifications stay intact during cell division, and may be inherited through the generations. Environmental influences can also impact this process (Reference, 2020). Essentially, epigenetics can influence whether certain genes are turned on or off. DNA methylation is a common form of epigenetic modification. This process consists of attaching small molecules called methyl groups to portions of DNA. When methyl groups are added to a particular gene, that gene is turned off or silenced (Reference, 2020). Moore et al., (2020) described genetics as "the study of heritable changes in gene activity or function due to the direct alteration of the DNA sequence." These alterations included mutations, deletions, insertions, and translocation. Conversely, researchers opined "epigenetics is the study of heritable changes in genetic activity or function that is not associated

with any change of the DNA sequence itself" (Moore et al., 2020). Biological embedding and the epigenome have been an area of focus in attempt to discern the relationship of the trauma and epigenetic paradox of early life experience. Essex et. al., (2013) surmised that biological embedding likely takes place when experience gets "under the skin and alters human biological processes; systematic differences in experience, under different nurturant conditions, lead to different bio-developmental states; the differences are stable and long-term; and these differences influence health, well-being, learning, or behavior over the life course." Underlying mechanisms of biological embedding are still being studied, but many researchers have now hypothesized that epigenetic processes are involved. Epigenetic methylation can modify the function of genetics and alter the way in which genes are expressed. The amalgamation of these findings presented evidence for a "biological embedding of early experience, or more specifically, the temporally remote correlates of early adverse experiences on the human epigenome and its regulatory role in the expression of specific genes, including genes that guide neurodevelopment" (Essex et al., 2013). Notably, Essex et al., (2013) research findings may be representative of the interplay between genetics and environment and the ability for experience and epigenetic variation to together impact salient developmental endpoints. Moore et al., (2020) suggested DNA methylation can be modified as a result of developmental mutations or environmental risk factors and mental illness is a typical byproduct. Research into DNA methylation has presented a detailed examination on epigenetic gene regulation and may offer possible therapeutic intervention targets for the treatment of neuropsychiatric disorders (Moore et al., 2020).

The prevalence of adverse childhood experiences has been linked to numerous lifetime health risk factors. The groundbreaking epidemiological study known as the Adverse

Childhood Experiences (ACE) Study, inaugurated together by the Kaiser Permanente Healthcare Clinic in California and the Centers for Disease Control and Prevention in 1995–1997, exposed an astounding correlation between childhood maltreatment, later-life medical complications, and early death. The CDC-Kaiser Permanente Adverse Childhood Experiences Study was one of the largest investigations of childhood abuse and neglect and household challenges and later-life health and well-being. The original ACE Study was conducted at Kaiser Permanente Healthcare and tested over 17,000 Health Maintenance Organization members. Subjects receiving physical exams completed confidential surveys regarding their childhood experiences and current health status and behaviors. ACEs were categorized into three groups: abuse, neglect, and household challenges. These categories were further split into multiple subcategories. Participant demographic information was available by gender, race, age, and education. ACEs prevalence was categorically organized. Results of the study affirm over half of participants report at least one, while one-fourth reported ≥2 categories of childhood adverse experiences. A graded relationship between the number of categories of childhood exposure and each of the adult health risk behaviors and diseases were analyzed. Respondents who endorsed four or more categories of childhood exposure, compared to those who had experienced none, had 4- to 12-fold elevated health risks for alcoholism, drug abuse, depression, and suicide attempt; a 2- to 4-fold increase in smoking, poor self-rated health, ≥50 sexual intercourse partners, and sexually transmitted disease; and a 1.4- to 1.6-fold increase in physical inactivity and severe obesity. The number of categories of adverse childhood exposures displayed a dose-response relationship to the existence of adult diseases including ischemic heart disease, cancer, chronic lung disease, skeletal fractures, and liver disease. There was a significant interrelation between the categories of adverse childhood experiences and persons with multiple categories of childhood exposure

that indicated a higher likelihood of multiple health risk factors later in life. The summation of the data demonstrated a strongly graded relationship between the breadth of exposure to childhood abuse or childhood household dysfunction and multiple elevated risk factors for numerous leading causes of death in adults (Felitti et al., 1998).

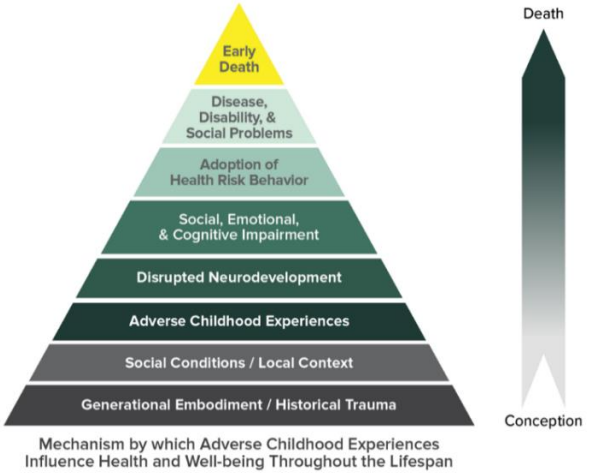
In a TEDMED Talk, Dr. Nadine Burke Harris (Harris, 2014) expanded on the vastly profound, long-term impacts of ACEs on one's physical health well into adulthood. In accordance with the Aversive Childhood Experiences Scale, she described individuals who endorsed ≥4 ACEs and had statistically significant worse health outcomes into adulthood, including two and half times greater risk of contracting chronic obstructive pulmonary disease and hepatitis. Individuals who endorsed ≥4 ACEs were also four and a half times more likely to suffer from depression and had twelve times the risk of suicidality. Further, Dr. Harris (2014) posited that individuals who endorsed seven or more ACEs had triple the risk of lung cancer and three and a half times the risk of ischemic heart disease – one of the top causes of death in the U.S. High doses of ACEs have been linked to neurological impairment and a higher likelihood of heart disease and cancer. The hypothalamic-pituitary adrenal axis is the body's stress response system that regulates stress hormones associated with fear responses. When this complex system is frequently activated by traumatic experiences, the result is often maladaptive and detrimental to health. Children and adolescents are particularly vulnerable to such risks as high levels of trauma can impact developing immune systems, hormone regulation, and even the way in which DNA is read and transcribed to RNA (Harris, 2014).

The ACE Pyramid (Figure 1), illustrates the conceptual foundations for the ACE Study. The ACE Pyramid highlights how ACEs are significantly related to increased likelihood of risk

factors for disease, death, and wellbeing throughout the life course *(About the CDC-Kaiser ACE Study |Violence Prevention|Injury Center|CDC, 2020)* .

Figure 2.

ACE Pyramid



It is remiss to speak of the esteemed ACEs study without mention of the rather accidental manner in which the study came about. Wylie (2020) reported that the study manifested as an unforeseen consequence of a Kaiser Permanente Healthcare weight-loss program that did not go as planned. During the mid-1980s, Vincent Felitti, founder of Kaiser Permanente's Department of Preventive Medicine, oversaw an obesity-treatment program. The program was initially successful for rapid weight loss. Within the first few years, the program began experiencing a high dropout rate primarily by subjects who had successfully lost a great deal of weight. In particular, one participant was a young woman who went from 408 pounds to 132 pounds in 51 weeks, but shortly after began rapidly regaining weight. Eventually, the participant reported a long history of severe childhood sexual abuse and disclosed she felt being overweight would protect her from future assaults. After a history of rapid weight fluctuation, she developed

primary pulmonary fibrosis, which caused severe weight loss, and ultimately lead to her death. In a statement, Felitti opined the patient “felt more comfortable because she knew she wouldn't live much longer—she felt her life sentence was finally over" (Wylie, 2020). This participant’s story spurred program directors to begin a more detailed examination into life histories of other patients in the obesity clinic. Data collected revealed that very few of the patients were overweight as children and, while the majority of overweight people gain pounds gradually over longer periods of time, they'd gained their weight abruptly, usually in response to a difficult or traumatic life event. Most notably during the analysis was the discovery of a pattern of childhood sexual abuse, trauma, family suicides, brutality, and other evidence of severely dysfunctional family relationships among the patient population in their clinic. One study of 286 obese people in Felitti’s program, found that half had been sexually abused as children. For these individuals, overeating and obesity were not the central problems, but attempted solutions for dealing with traumatic experiences (Wylie, 2020).

Research has revealed maltreatment, particularly early in life, alters trajectories of brain development to affect sensory systems, network architecture, and circuits involved in detection of threat, emotional regulation, and reward anticipation. Teicher et al., (2016), found maltreated and non-maltreated individuals with the same psychiatric diagnosis should be clinically differentiated, as the maltreated subgroup displayed a unique eco-phenotype with distinct clinical, neurobiological, and genetic features which supports the epigenetic model of stress exposure. Gurre et al., (2019) posited that traumatic stressful events were associated with common and unique differences in symptoms, neurocognition, and structural and functional brain parameters and was associated with earlier puberty by physical features and brain maturation. Mendle et al., (2011) explained how trauma of child sexual abuse introduces both

physiological and psychological outcomes for children by advancing maturation through activating the hypothalamic-pituitary adrenal (HPA) and other axes prematurely. These stress-induced modifications in hormones explain the timing of maturation, as well as aggressive and sexualized behavior that tends to be displayed in childhood sexual trauma survivors. In conjunction with this, studies have confirmed dysregulation of the HPA axis among females with a history of sexual abuse (Mendle et al., 2011). Prevention of early life adversity was indicated as a critical component to improving health and life outcomes into adulthood (Merrick et al., 2018). Comprehension of the relevance of frequency and long-term effects of childhood abuse to medical problems in adulthood has been proposed as a rudimentary component of adult clinical care. These connections play a key role, as the leading causes of morbidity and mortality in the United States have been directly related to health behaviors and lifestyle factors; which are commonly referred to as the "actual" causes of death. When accounting for the role of abuse and other potentially damaging childhood experiences in the development of these risk factors, one may deduce that childhood exposures should be recognized as the basic causes of morbidity and mortality in adult life (Felitti et al., 1998).

Trauma exposure often leads to sleep deprivation. Disturbed sleep is a common occurrence after a significantly traumatic event, and a prominent feature of posttraumatic stress disorder. Sleep deprivation has been found to cause complex effects on affective dimensions and modalities of perceived pain in healthy subjects as well as subjects enduring major depression. Varied connections between mood and pain regulation in patients with chronic somatoform pain has been a subject of research on the mind-body connection. Sleep deprivation has also been linked to neurobiological differences between regulation of emotions and internal pain processing (Busch et al., 2012). Data has indicated that difficulty initiating and maintaining

sleep often results in a lack of restorative sleep which leads to potential compromise of immune system responses to threat as well as the brain and body's ability to regulate stress hormones. Long-term effects of restorative sleep deprivation have been shown to result in increased levels of physical and mental illness. When these sleep symptoms are endured repeatedly over time, the effects have been compounding, subjecting individuals to higher levels of stress response, physical illness, and thus making them all around more vulnerable to disease. Palagini et al., (2015) identified early life stress exposure as playing a key role as a predisposing factor for vulnerability to hyperarousal reactions to negative life events, which can contribute to the development of chronic insomnia. Multiple studies have indicated the conspicuous role of childhood stress including sexual, physical, or emotional abuse, emotional or physical neglect, or parental loss, in the production and development of disease of stress-related disorders including depression and insomnia (Palagini et al., 2015). Schernhammer et al., (2001) composed a longitudinal study among a large sample of nurses who worked rotating night shifts. Their data indicated the risk of breast cancer was statistically significantly higher in postmenopausal women who worked for 30 or more years on rotating night shifts, compared with those who never worked rotating night shifts. Among premenopausal women, Schernhammer et al., (2001) found a heightened breast cancer risk of 23% after 1–14 years of shiftwork. This study further supports the life-threatening, detrimental effects sleep deprivation and disrupted circadian rhythms can have on physical health.

In his TED talk, Walker (2019) lectured that sleep disruption is a contributing factor to Alzheimer's disease, leads to reduced testosterone levels in males, and impairs the female reproductive system. Notably, sleep impairment can take a remarkable toll on one's cardiovascular system. Walker (2019) described a "global experiment performed on 1.6 billion

people across 70 countries, twice a year, and it's called Daylight Savings Time." This natural experiment has illustrated the profound impairments one hour less of sleep can have on an individual's health. During springtime daylight savings when there is one hour of sleep loss data showed an average of 24% increase in heart attacks the next day. In the fall when individuals gain an hour of sleep, data shows a 21% reduction in heart attacks the next day. Similar profiles are shown for car crashes and suicide rates during daylight savings. Walker (2019) explained the remarkable impact sleep loss has on the immune system. Humans have "natural killer cells" designed to identify dangerous, unwanted elements and eliminate them. These cells have the ability to destroy cancerous tumors. Ideally, humans need a potent set of these natural killer cells to remain healthy. Walker (2019) discussed a sleep experiment on healthy adults which restricted individuals to four hours of sleep for one night. After the loss of sleep participants' immune cell activity was measured and it displayed a 70% reduction rate in natural killer cells after one night of decreased sleep. These reduced cell levels marked a state of immune deficiency. Results of this experiment were important, as they highlighted the significant links between short term sleep deprivation and risks of developing multiple forms of cancer including cancer of the bowel, cancer of the prostate, and cancer of the breast. The link between sleep disturbance and cancer has become so significant that the World Health Organization has declared any form of nighttime shiftwork as a potential carcinogen because of disrupted circadian rhythms. Walker (2019) detailed that "lack of sleep will erode the very fabric of biological life itself; your DNA genetic code." He went on to describe one study that tested a group of six healthy adults that were limited to six hours of sleep a night for one week and then measured the change in genetic activity profiles relative to when the same individuals were getting eight hours of sleep a night. Results of the study revealed 711 genes were distorted. The

study also found that approximately half of the genes increased in activity, while the other half decreased. Genes that were switched off due to sleep deprivation were associated with immune system deficiency. The other half of genes that were upregulated by sleep deprivation were associated with the promotion of tumors, long-term chronic inflammation in the body, genes associated with stress, and cardiovascular disease. Walker (2019) expressed that loss of sleep interferes with "the DNA nucleic alphabet that spells out your daily health narrative." He went on to emphasize that "We know this from epidemiological studies across millions of individuals. There's a simple truth: the shorter your sleep, the shorter your life." The distinct correlation between psychological trauma and sleep disturbance and the amalgamation of accompanying symptomology highlight the short-term and long-term significance of the role sleep loss plays in poor health outcomes, both physically and psychologically in the aftermath of trauma exposure.

Research has continued to find high rates of comorbidity between psychological trauma and physical illness. It has become relatively well known that posttraumatic stress disorder does not occur in a vacuum, but rather, it is often further complicated by multiple pathologies. Typical sequelae proceeding a traumatic event have often included chronic pain and posttraumatic stress disorder. Because many forms of trauma can leave chronic pain in its wake, the interplay between posttraumatic stress disorder and physical pain has become an area of concern for many survivors of trauma. Van der Kolk (2015) described "After trauma the world is experienced with a different nervous system. These attempts to maintain control over unbearable physiological reactions can result in a whole range of physical symptoms, including fibromyalgia, chronic fatigue, and other autoimmune diseases." He went on to opine that from a clinical perspective "it is critical for trauma treatment to engage the entire organism, body, mind, and brain."

Burke et al., (2016) defined chronic pain as pain persisting for longer than 3 months and the average duration of pain in chronic pain patients is 7 years and noted the nature of chronic pain often resulted in significant emotional distress and poorer quality of life. Research evidence has continued to find a substantial association between early-life stress and adversity with an elevated occurrence of chronic pain in later life. A meta-analysis reported subjects who endorsed child abuse or neglect had increased levels of pain symptoms compared to those not exposed to such trauma, and similarly, that chronic pain subjects were more likely to report childhood trauma. Childhood adversity is associated with chronic pain in later life (Burke et al., 2016). Studies have provided evidentiary support regarding the complex interactions between early life events and gene expression, how this may alter brain development, and how such interactions were theorized to underlie the connection between early-life stress and pain later in life. "Early-life stress has been significantly shown to result in numerous abnormalities that may account for maladaptive development and/or functionality within pain circuitry, enhancing susceptibility to the development of chronic pain in later life" (Burke et al., 2016).

Nusslock and Miller (2016) reported research that shows childhood adversity sensitizes the immune cells that initiate and sustain inflammation. These researchers described that "maltreated and disadvantaged children are disproportionately exposed to pollutants, second-hand smoke, and high-fat and high-sugar diets, along with psychosocial stressors like family instability, insensitive caregiving, and neighborhood violence" (Nusslock & Miller, 2016). The cortico-amygdala neural circuit, a part of the brain that supports vigilance for, and responses to threat has also been linked to biophysiological effects of trauma. Several salient findings regarding early life adversity indicate it often leads cortico-amygdala neural circuitry sensitization. When considered together, the cortico-amygdala and inflammatory sequelae of

childhood adversity play a major role in growing literature that suggests both are key factors of an "integrated, bidirectional network that detects threats to well-being, and mobilizes behavioral, physiologic, and inflammatory resources for coping" (Nusslock & Miller, 2016). Childhood adversity effects reward sensitivity in multiple ways, however, literature implies a potential mechanistic role for inflammation. Reward sensitivity blunting is a component of a generalized pattern of adaptations to infection, mediated by inflammation. Adaptations such as these are commonly known as sickness behaviors, along with anhedonia, dysphoria, fatigue, psychomotor slowing, and inactivity. According to Nusslock and Miller (2016) "Sickness behaviors have evolutionary adaptive qualities, maximizing an organism's chances of surviving infection by diverting energetic resources to the immune system, and minimizing contact with other pathogens and predators." The researchers hypothesize that by decreasing reward sensitivity and increasing dysphoric feelings, inflammation promotes high-risk behaviors with poor health outcomes. Adverse childhood experiences have been linked to increased rates of cigarette smoking, excessive alcohol consumption, drug misuse, physical inactivity, and high-fat eating. Severe childhood adversity often yields a profuse amount of medical challenges throughout the lifespan. "All of these conditions develop through etiologically complex transactions between genetics, lifestyle, and the environment, as mediated via dysregulation of multiple physiological systems" (Nusslock & Miller, 2016).

Multiple barriers have impeded research capabilities into the study of the co-occurrence of trauma and chronic pain. Despite the frequent use of the term "chronic pain" in a clinical context, this is actually not a formal diagnosis. Early versions of the *Diagnostic and Statistical Manual (DSM)* had difficulty defining complex criteria for pain related disorders. The number of poorly defined diagnostic criteria for chronic pain brought forth challenges in dissecting the

comorbidity between disorders. Sharp and Harvey (2001) are pioneers in the development of research into this phenomenon. Their studies have concluded that there are multiple pathways by which chronic pain and posttraumatic stress disorder can be mutually maintaining conditions. These researchers proposed that there are several pathways in which both disordered conditions can be involved in the escalation of symptomology and stress response after experiencing trauma. Sharp and Harvey (2001) reviewed extensive literature in regards to what factors maintain posttraumatic stress disorder and chronic pain symptomology and proposed a number of processes believed to maintain these two conditions. Factor analysis revealed *Attentional biases* toward trauma-related and pain-related inputs as the first factor. The researchers theorized that pain sensations may act as trauma reminders and induce further attentional biases in a circular manner. Second, *anxiety sensitivity* was hypothesized as a potential maintaining factor of comorbid posttraumatic stress disorder and chronic pain. Anxiety sensitivity, the fear of arousal-related sensations brought on by beliefs that these sensations are threatening, was postulated to promote anxious interpretation of bodily sensations and physical pain in comorbid conditions. A third maintaining factor was hypothesized as *persistent reminders of the trauma*. Although events that trigger the reexperience of symptoms (a posttraumatic stress disorder trait), Sharp and Harvey (2001) proposed that the sensations accompanied with pain likewise may be interpreted as triggers of traumatic experiences, especially when considering the link between the traumatic event and pain-producing physical injuries. The fourth maintaining factor was hypothesized as *avoidant coping style* in relation to comorbid pain and posttraumatic stress disorder. Even though avoidance of specific physical activities may be required for certain physical ailments, extensive avoidance of pain cues may result in physical deconditioning and distress while avoidance of trauma related cues may inhibit fear extinction and reprocessing of

safe cues. *Depression and reduced levels of behavioral activity* were listed as the fifth maintaining factor. These components were found to serve as mutually maintaining factors by adding to disability in pain individuals while also hampering exposure to trauma cues. *Pain perception* was listed as the sixth maintaining factor. It was theorized that pain perception, heightened by anxiety, likely operates in a feed-forward fashion, raising levels of perceived pain, emotional distress, and disability in patients with a comorbid diagnosis. Lastly, Sharp and Harvey (2001) recognized that both posttraumatic stress disorder and chronic pain demand *cognitive resources* and proposed that these demands challenge an individual's ability to take part in more adaptive strategies for coping with distress and disability.

Alexander et al., (1998) evaluated the relationship between prior sexual and/or physical abuse and health care usage in women with fibromyalgia, and revealed variables that may influence this relationship. Results of the study found that 57% of individuals reported a history of sexual and/or physical abuse. Compared to non-abused subjects, abused subjects reported higher numbers of utilization of outpatient health care services for problems other than fibromyalgia and higher use of pain medication. Subjects who had been abused also endorsed significantly greater levels of pain, fatigue, functional disability, and stress. These findings indicated a relation among fibromyalgia patients between sexual/physical abuse and increased use of outpatient health care services and medications for pain. The researchers hypothesized this association may be affected by clinical symptoms, functional disability, psychiatric disorders, stress, and abnormal pain perception.

Research has demonstrated strong connections between childhood maltreatment and physical health ailments that include dissociative symptoms and fibromyalgia syndrome.

In their study, Bohn et al., (2013) found that on average, patients who had endured childhood maltreatment reported high levels of somatoform dissociative symptoms and moderate levels of somatic symptom severity and depression. Somatoform dissociative symptoms and emotional abuse were moderately correlated.

Ciccone et al., (2005) proposed that according to the trauma hypothesis, women with fibromyalgia have a higher likelihood to report a history of sexual and/or physical abuse than women without fibromyalgia. Results of their study revealed that except for rape, sexual and physical abuse were reported equally often by women in fibromyalgia and control groups. Women who reported rape were 3.1 times more likely to have a fibromyalgia diagnosis than women who did not report rape. Their study also found that women with fibromyalgia were more likely to have posttraumatic stress disorder symptoms as well as posttraumatic stress disorder diagnosis. When contrasted with the trauma hypothesis these results indicated posttraumatic stress disorder was more prevalent in the fibromyalgia group. Ciccone et al., (2005) discerned that chronic stress in the form of posttraumatic stress disorder but not major depressive disorder may act as a mediator in the relationship between rape and fibromyalgia.

Cichowski et al., (2017) studied the prevalence of chronic pain conditions among U.S. female veterans with a history of military sexual trauma to those without a history of military sexual trauma. Results of this multivariate model revealed an association between military sexual trauma and chronic pain conditions including irritable bowel syndrome, chronic pelvic pain, back pain, chronic joint pain, fibromyalgia, dyspareunia, chronic abdominal pain, and headaches. Drug abuse and overdose were also associated with military sexual trauma. Cichowski et al., (2017) concluded that history of military sexual trauma in females was significantly associated with chronic pain diagnoses.

Pegram et al., (2017) sought to clarify the cognitive and social mechanisms by which traumatic events may affect pain-related outcomes. They hypothesized that suppression of intrusive thoughts and the experience of social constraints may link traumatic experiences with pain outcomes. Pegram et al., (2017) concluded that this study added to trauma, emotion, and chronic pain literature by proposing a theoretical model by which the experience of potentially traumatic events throughout one's life impacts pain-related outcomes. They also concluded that suppressing thoughts after traumatic experiences may exacerbate pain, and the combination of high social constraints against disclosing one's trauma and suppressing one's thoughts can be significantly damaging.

Lippard and Nemeroff (2020) also cited early-life adversity as a factor in increased vulnerability to numerous major medical disorders, including coronary artery disease and heart attacks, cerebrovascular disease and stroke, type 2 diabetes, asthma, and certain forms of cancer. Studies show that survivors of child abuse and neglect typically have a significant decrease in life expectancy. Further, Lippard and Nemeroff (2020) elaborated that emotional abuse and neglect in childhood are more likely to be undocumented clinically, but this form of maltreatment also renders harmful health outcomes, independently of physical abuse, neglect, or sexual abuse. Inflammation and other immune system disruptors, hypothalamic-pituitary adrenal (HPA) axis changes, genetic and epigenetic expressions, and structural and functional alterations in brain images have all been significantly linked to maltreatment in childhood. Maltreatment during childhood was also associated with increased body mass index in 483 subjects who were identified as being on the psychosis spectrum. Subjects experiencing depression and bipolar disorder have also been found to display heightened levels of inflammatory markers. Alterations of the HPA axis and other circuits that regulate endocrine, behavioral, immune, and autonomic

responses to stress is another mechanism found to increase risk of mood disorder and disease. Early life adversity likely enhances sensitivity to the biological effects of life stressors. These researchers elaborated on the interplay between genetic predisposition and childhood maltreatment as heightening risk for mood disorders and disease and posited gene-by environment interactions influence disease vulnerability (Lippard & Nemeroff, 2020). Epigenetics has been found to be profoundly impacted by childhood maltreatment and such modifications have been linked to suicide completion, altered stress hormone systems, and illness severity. Further, associated epigenetic changes related to childhood maltreatment support gene-by-childhood maltreatment interactions, including epigenetic modifications as a risk for mood disorders and in illness course in adulthood. Lippard and Nemeroff (2020) discussed how multiple studies have revealed that maltreatment during childhood is associated with decreased volumes of gray matter in certain areas of the brain. They also describe how several other studies have found an association between childhood maltreatment and decreased structural integrity of white matter in the same regions of the brain as well as smaller hippocampal and prefrontal cortical volumes. These studies implicate mechanisms at play that are capable of superseding diagnostic boundaries and posing heightened risk for psychopathology and genetic variation that may connect neurobiology, childhood maltreatment, and vulnerability to pernicious outcomes. The intercommunication among adversity early in life, serotonin transporter promoters, and disease vulnerability and illness course has been supported by many studies. Data such as these highlight the potential of genetic coding to contribute to long-term structural changes in the brain in the aftermath of childhood maltreatment (Lippard & Nemeroff, 2020).

Kalin (2020) reviewed a unique study performed in the emergency department of Grady Memorial Hospital in Atlanta, Georgia. The analysis examined immune related predictors for

developing posttraumatic stress disorder in acutely traumatized adults. Researchers utilized a prospective longitudinal design to evaluate a relation between immune factors assessed in close proximity to trauma with long-term effects of trauma. The study found decreased amounts of biological markers which were predictive of a chronic posttraumatic stress disorder outcome (Kalin, 2020).

Contributions to Practice

In order to combat the life altering effects of psychological trauma more research related to effective prevention and intervention is still needed. Felitti et al. (1998) suggested more training is needed to assist medical and public health practitioners in the understanding of how social, emotional, and medical problems are intertwined throughout the lifespan. Such measures could provide clinicians outside of the mental health realm with the competence and skills to inquire and respond to individuals who acknowledge a history of significantly unresolved trauma (Felitti et al.,1998). Increased awareness of the frequency of life altering consequences of adverse childhood experiences and psychological trauma may also lead to improvements in health promotion and disease prevention programs. Since Felitti et al.'s (1998) proposition, a shift toward an interdisciplinary approach to patient care has been established. Although not all intuitions have adopted this method of treatment, many have begun to view mental illness from a more whole health perspective that synthesizes both medical and psychological approaches to care. Continuing to utilize this approach could have promising outcomes in the treatment of psychological trauma, chronic pain, and disease.

Lastly, and of vital note, mental health practitioners must employ deductive reasoning for diagnostics and intervention. Unlike medical practitioners, mental health clinicians are unable to

utilize tests such as radiographs or blood work to clearly indicate the presence of abnormalities or disease. However, if mental health clinicians can obtain better understanding of how medical conditions are linked to psychological trauma and mental illness, they may better assist patients in understanding this complex system as well. As Winch (2014) described in his TED Talk: "You put a bandage on a cut or take antibiotics to treat an infection, right? No questions asked. In fact, questions would be asked if you *didn't* apply first aid when necessary." He went on to illustrate this from a mental health perspective: "So why isn't the same true of our mental health? We are expected to just "get over" psychological wounds…emotional injuries can be just as crippling as physical ones." Mental illness is still largely stigmatized and unrecognized in modern society. Individuals are significantly more likely to seek treatment for medical conditions as opposed to psychological conditions. Physical and psychological pain are not mutually exclusive, but rather exist in a circular, connected pattern. If a greater understanding of this concept spreads, perhaps it would promote the destigmatization of mental illness and advance effective interventions to thwart the harmful effects psychological trauma has not only on the mind but on the body as well.

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