Alamdari and Laganà. J Geriatr Med Gerontol 2015, 1:1
ISSN: 2469-5858

Journal of
Geriatric Medicine and Gerontology

Research Article: Open Access

The Relationship of Older Adults' Physical Pain to Depression and Post-Traumatic Stress Disorder (PTSD): A Review

Golnar Alamdari[1] and Luciana Laganà[2]*

[1]*Graduate School of Education and Psychology, Pepperdine University, USA*

[2]*Department of Psychology, California State University Northridge, USA*

***Corresponding author:** *Luciana Laganà, Department of Psychology, California State University Northridge, 18111 Nordhoff Street 8255, Northridge, California 91330, USA, Tel: 818-677-2827, E-mail : Luciana.Lagana@csun.edu*

Abstract

Background: Physical pain is very common in older age and is often accompanied by depressive as well as PTSD symptomatology. Many conceptualizations of the comorbidity of pain with depression and with PTSD exist, but they need to be tested on older adult populations.

Purpose: This article covers existing literature on the relation between depression and pain in older age, as well as between older adults' PTSD and pain. Additionally, several physiological, cognitive, and behavioral conceptualizations of why depression and PTSD are often related to pain are presented.

Methods: The PsychInfo, PubMed, and Google Scholar databases were searched for relevant articles by utilizing the following terms in combination with chronic pain (as well as with pain alone): aging, older adults, elderly, depression, depressive, post-traumatic stress, and PTSD. Additionally, Thomson Reuters Web of Science database searches were conducted using the terms "elderly (and older adults) pain depression PTSD." This review includes various articles that conceptualize the pain-depression, pain-PTSD, and pain-depression-PTSD links, yet, due to space limitations, the review is not comprehensive. Several pertinent reviews are referenced throughout the paper for readers interested in obtaining additional information in this area.

Results: Depression and PTSD are comorbidities for pain at any age, and are characterized by several and often complex mechanisms that can exacerbate pain.

Conclusion: The comorbidity of pain and factors such as depression and PTSD in older age should be addressed in more research studies, as few investigations are available in this area on the general population of older individuals. This is particularly the case for non-Caucasian older adults living with chronic pain.

Keywords

Chronic pain, Older adults, Elderly, Depression, Post-Traumatic stress disorder, Psychopathology, Comorbidity

Introduction

In a high quality research study conducted earlier this year, Outcalt, Kroenke, Krebs, et al. [1] emphasized that depression and post-traumatic stress disorder are often present in individuals living with chronic pain and typically have negative consequences on both the experience of pain and health outcomes, yet, the specific nature of the pain-depression-PTSD link remains unclear. This is especially applicable to older adults, a population that has seldom been studied on this topic. As detailed later, these three variables appear to share several common physiological, neurological, and immunological mechanisms; this makes researching them in a simultaneous fashion a challenging yet important task. To shed some light in this area, the present article incorporates a discussion of older adults' depression and PTSD in relation to pain. It also includes possible explanations for the comorbidity of pain experienced at any age with these two important variables. Due to space limitations, this is not a comprehensive review of the literature published on the topic of depression and pain, or PTSD and pain. However, several review articles are referenced for readers interested in additional information in this area.

Pain in older age is a very critical subject due to its significant negative impact on the rapidly growing older adult population. Indeed, with the United States (U.S.) population of individuals over the age of 65 growing rapidly, this country is observing a decrease in fertility rates and an increase in life expectancy [2]. The concurrent growth in the older adult population and decline in fertility rates contribute to the relatively rapid pace of growth in the aging population within the U.S., which, as predicted two decades ago, will observe a sharp increase from 7 percent to 14 percent in the older adult population within just 69 years [3]. Astoundingly, this figure could be an underestimation of the size of the older population in the next few decades, especially in view of recent medical advances.

Among the most prevalent diseases in older age are non-communicable diseases [4,5], which are comprised of any chronic or acutely developed diseases that are not spread from one person to another [6]. Non-communicable diseases include cardiovascular diseases, cancer, long-term respiratory diseases, diabetes, and fibromyalgia [6,7]. Most relevant to the focus of this article, chronic pain is a common comorbid condition among older adults suffering from non-communicable diseases including (but not limited to) diabetes [8], arthritis [9] and asthma [10]. As such, non-communicable diseases are unfortunately anticipated to inflate the incidence and prevalence of chronic pain globally [11].

Underlying the importance of this discussion, the prevalence of chronic pain is positively correlated with age, as complaints of pain related to factors such as joints and nerves are more common in older

ClinMed International Library

Citation: Alamdari G, Laganà L (2015) The Relationship of Older Adults' Physical Pain to Depression and Post-Traumatic Stress Disorder (PTSD): A Review. J Geriatr Med Gerontol 1:007

Received: December 01, 2015: **Accepted:** December 29, 2015: **Published:** December 31, 2015

age [12,13]. Among older adults residing in nursing institutions, the prevalence of chronic pain ranges between a very high 45% and a staggering 80% [14-16]. A category of non-communicable diseases commonly experienced in older age comprises mental health conditions such as depression and PTSD [7], increasing the likelihood that many older adults living with chronic pain also have to cope with severe psychopathology. Moreover, although a review of the factors that serve as barriers to proper medical and pain care is beyond the scope of this article, it is important to address them briefly. They include having health insurance problems [17], lower educational levels [18], as well as an ethnic minority background and low socio-economic status [19]. Furthermore, an under-investigated yet important potential risk factor for pain is perceived racial discrimination, which has been related to higher pain reports of older African-American male veterans [20].

The foundations of future empirical geriatric studies in this area could be found in many theories and conceptualizations of the pain-depression and pain-PTSD links, as highlighted in the following sections. Gerontologists and scholars from all scientific fields who are engaged in geriatric research are strongly encouraged to conduct studies aimed at 1) verifying whether the following conceptualizations hold true in older age and, if not, which variations occur due to advanced age, and 2) discovering ways in which the mechanisms hypothesized in such conceptualizations could be best manipulated, with the goal of decreasing the comorbidity of physical pain, depression, and PTSD in older age as well as their deleterious impact on older adults' quality of life.

The Comorbid Relationship of Depression and Pain

Introduction

Major depressive disorder is one of the most widely depressive manifestations examined in the literature. The 12-month prevalence rate of a major depressive episode among people 50 years of age and older is about 5.5% [21]. Furthermore, there exists a disparity between the prevalence of depression among older men and women that is consistent with the well-established finding that women experience major depression about twice as often as men [22]. Thus, older women should be especially targeted in research in this area.

Pain may present itself in a variety of ways such as a pathological condition (as previously mentioned), an undiagnosed medical condition, a neurological condition such as multiple sclerosis, or a somatic condition such as cancer or rheumatoid arthritis [23]. The comorbidity rate of depression and chronic pain typically ranges between 30% and 60% [24]. Research indicates a higher incidence of reported somatic complaints such as pain among individuals diagnosed with depression [25,26]. On the other hand, literature also supports a link between the physical as well as the psychological distress of conditions of chronic pain and a higher likelihood of developing depression [27,28]. Specifically, it has been documented that more than 50% of individuals experiencing chronic pain report clinical symptoms of depression [29].

The above-mentioned significant rates of depression-pain comorbidity have created a platform from which researchers have explored the direction of influence between depression and pain. Despite speculations regarding the direction of influence between these two variables, the factor that remains constant is the negative effect that the comorbidity of depression and physical pain have on each other. Specific to the older adult population, depression treatment outcomes are often negatively affected by pain. An example of relevant research is a longitudinal study on the course of older patients' depression, in which the experience of pain significantly weakened the probability of recovery, as 47% of those with major depressive disorder recovered, while only 9% of older adults with comorbid major depressive disorder and pain did [30]. Furthermore, pre-existing medical conditions that lead to symptoms of chronic pain can be exacerbated by the presence of major depressive disorder. For instance, conditions such as fibromyalgia, a musculoskeletal disorder that manifests through a long-term pervasive muscular pain, may be triggered or worsened by depression [31,32].

Most of the explanations listed in the following sections for both depression and PTSD have not been formally tested on older adults and include samples that contain both older and younger adults, thus not allowing for generalizations of the results to geriatric populations.

Potential Explanations of Comorbidity of Depression and Pain

This section contains a summary of some of the well-known conceptualizations of the relationship between depression and pain. As already mentioned, due to space limitations, this review is not meant to be comprehensive. For the interested reader, published reviews in this area include articles by Blackburn-Munro & Blackburn-Munro [23], Bair, Robinson, Katon, and Kroenke [33], as well as Brooks, Kominek, Pham, and Fudin [34].

The diathesis-stress model

The Diathesis-Stress Model [35] postulates that the source of depression in cases of chronic pain is traced to a predisposition toward depression that is developed at the onset of stressful stimuli, such as chronic pain. What makes this model unique is its integration of biological, cognitive, and behavioral elements in combination with or independently reacting to stressful stimuli. The sensitivity to these stimuli in inducing the onset of depression depends on individual variations and predispositions. The behavioral and cognitive aspects of the model depend on the source and onset of depression, and are significantly influenced by chronic pain. For example, from a behavioral perspective, chronic pain may lead to an inability to engage in activities and thus can decrease the experience of positive reinforcement, resulting in negative affect and depression. From a cognitive perspective, chronic pain may present the individual with situations within the medical system in which attention and responses by professionals within the medical system may be perceived as dismissing, serving as a stressor in the development of depression [35,36].

Brain abnormalities

The literature on physiological differences (detected through neuroimaging) in brain structure and function among individuals with depression, neuropathic pain, and fibromyalgia indicates the existence of vast similarities in recorded brain abnormalities. Specifically, brain areas such as the dorsolateral prefrontal cortex, medial prefrontal cortex, lateral orbital prefrontal cortex, insula, nucleus accumbens, amygdala, hippocampus, and thalamus have been associated with functional or structural abnormalities. The results of such brain abnormalities may lead to a bidirectional relationship between chronic pain and depression, as they influence the perpetuation and severity of one another [37]. For instance, electrophysiological, biochemical, and imaging reports suggest that abnormalities in both the function and structure of the amygdala - in cases of chronic pain and symptoms of depression as well as anxiety, may increase the amygdala's sensitivity to experiences of pain [38]. According to Rainville, Bao, & Chrétien [39], negative perceptions and feelings that are characteristic of major depressive disorder also serve to augment the sensation and recognition of pain. Similarly, abnormalities in the structure and function of the dorsolateral prefrontal cortex in major depressive disorder and chronic pain disturbs the top-down process of emotion regulation in depression and pain regulation, altering sensations of pain within pain pathways, cognition, and ability to cope [40-43].

Regarding individuals with major depressive disorder and chronic pain, research exists on the simultaneous over-activation of the limbic system and on the effects of the prefrontal structures on decreasing dopaminergic activity due to an increased distress alert [37]. Alterations in the ventral striatum and nucleus accumbens are reported to serve an important role in the body's stress and pain response, as well as in the reward and pain sedation mechanisms

[44-46]. The nucleus accumbens communicates with the prefrontal cortex gathering signals regarding cognition, emotional information from the amygdala, and information regarding the context of stimuli from the hippocampus [46]. Similarly, the nucleus accumbens regulates the ventral tegmental area's dopaminergic activity. The findings of neuroimaging reports on the relationship between the nucleus accumbens and the ventral tegmental area suggest that there may be a disruption in functioning between the nucleus accumbens and ventral tegmental area in individuals with major depressive disorder and chronic pain [47,48]. Over-activation of the amygdala, subgenual anterior cingulate cortex, and ventral medial prefrontal cortex could disrupt dopaminergic activity within the ventral tegmental area, resulting in a skewed reward mechanism, cognitive impairments, reduced desire to experience novel stimuli, and impaired pain management [44,45,47-49]. Furthermore, regarding people's susceptibility to experiencing chronic pain related to major depressive disorder, Bär et al. [50] highlighted the significance of the location of pain in individuals with depression, while cerebral blood flow in brain structures has been found to affect the emotional regulation of pain [51].

Hypothalamic-pituitary-adrenal axis mechanism

The activation of the hypothalamic-pituitary-adrenal (HPA) axis associated with the limbic and autonomic systems comprises a conceptualization that could explain a potential mechanism contributing to the onset of fibromyalgia and neuropathic pain as well as depression [37]. Richards & O'hara [36] reviewed various studies that suggest an overstimulation of the HPA axis in both depressed and chronic pain conditions, defined by a greater level of cortisol stimulation and a decrease in morning cortisol suppression [52-55]. Indeed, diseases such as fibromyalgia and depression may be triggered by stressors that stimulate the negative feedback loop within the HPA axis and prompt the production of corticotrophin-releasing hormone (CRH) and arginine vasopressin (AVP) released by the hypothalamus, which signals the release of adrenocorticotropic hormone (ACTH) through the pituitary gland. As a result, the secretion of ACTH activates the adrenal release of cortisol [56,57]. The hormone cortisol is a glucocorticoid, also known as the stress hormone [58], and typically functions by reducing CRH and ACTH production, constricting any form of action within the body, including immune function [56,59]. Exposure to a stressor for a prolonged period of time may result in the disruption of the HPA axis and fluctuating cortisol levels, affecting experiences of pain, as well as lethargy and mood [60,61].

Inflammatory mechanism

It is plausible that an impaired HPA axis - resulting in fluctuating levels of cortisol shared in chronic pain and depression patients - is not the only biological mechanism aiding their comorbidity, as a disruption in monoamine transmission could also contribute to it, in combination with HPA axis disruption [62]. An abundance of pro-inflammatory proteins such as cytokines may be involved in the comorbidity of pain and depression [62,63]. Cytokines are known to relay information to cells regarding the intensity and duration of response to an infection or disease. Unlike hormones whose secretion is regulated by glands, cytokines are secreted by immune cells within and outside the central nervous system and are regulated by feedback loops [64].

Among the different variations of cytokines, the molecules TNF-α, IL-1, and IL-6, among others, are associated with pro-inflammatory functions and are known as pro-inflammatory cytokines (PICs) [65]. PICs play an important role in the "sickness response" [66], which is a natural mechanism intended to enhance survival through an increased constraint of movement and conservation of energy for the body's defensive purposes. This response includes physiological symptoms similar to the flu, such as elevations in body temperature as well as alterations in the regulation of the HPA axis and sympathetic nervous system while affecting secretions of hormones such as serotonin. The end result involves changes in behavior similar to symptoms associated with depression, including a heightened experience of pain, reduction in social interaction and in sexual activity, as well as increased sleep [66-68]. Because many behavioral symptoms of the sickness response are similar to those of depressive symptomatology, researchers have examined the relationship between PICs and depression, establishing a theory that incorporates a patho-physiological approach.

In a study targeting the older adult population via sampling over 3,000 physically healthy older adults, an elevated level of PICs IL-6, TNF, and/or C-reactive protein was found to be correlated with a heightened risk of depression by over double [69]. Along with the variety of behavioral symptoms associated with the sickness response and the characteristics of depression, a heightened experience of pain has been found. After all, the sickness response is an essential response in increasing an organism's chance of survival. Researchers have studied the central nervous system's immunity reaction through the stimulation of neuroglial cells such as astrocytes and microglial cells to respond to physical threats such as inflammation or injury [66]. The specific function of astrocytes, limited to function within the brain and spinal cord, is to manage neural communication; however, the specific function of microglial cells parallels the role of a macrophage, as these cells remove dead neurons at the location of injury [70]. Stimulated neuroglial cells appear to function to generate various molecules such as PICs within the central nervous system as a response to neural signals from peripheral PICs stimulated by an immune stressor [71]. In a study on 81 individuals diagnosed with fibromyalgia against 32 healthy individuals, participants suffering from fibromyalgia had higher levels of the IL-8 and scored higher on the Hamilton Depression Rating Scale than the control group [72]. These findings suggest the existence of a relationship between an increased presence of cytokine and depressive symptoms as well the exacerbation of pain.

The Comorbid Relationship between PTSD and Pain

Introduction

Mental health conditions such as PTSD greatly affect the older adult population and, in particular, older women. The prevalence of PTSD in older age falls within the 1.5% to 4% range [73], with the subclinical manifestation of PTSD in older men falling within the 7% to 15% range [74]. The likelihood of exhibiting symptoms characteristic of PTSD is twice as high for women than men [75,76], highlighting the need for research in this area. Some scholars have speculated that this disparity may be due to a woman's higher risk of exposure to trauma like sexual abuse or assault that could lead to PTSD [77,78]. Whatever the reason, it is essential to study PTSD in relation to pain among older adults, because the prevalence and epidemiology of the comorbidity of PTSD and chronic pain have not yet been widely explored in older age groups. Researchers have found it particularly difficult to differentiate the source of pain and whether its onset was a result of the same event that prompted the traumatic experience; however, recently there has been a growing interest in recognizing and assessing the PTSD-pain relationship [79]. According to the National Co-morbidity Replication Survey, 7.3% of the individuals experiencing chronic back pain also exhibit symptoms of PTSD [80]. In another epidemiological study from the Canadian Community Health Survey, differences were found in the comorbidity rate of chronic pain and PTSD related to specific pain conditions, as these rates were 7.7% among individuals with fibromyalgia and 46% among individuals with back pain [81].

Potential Explanations of Comorbidity of PTSD and Pain

As was the case for the above coverage of the pain-depression link, this section comprises only a selection of the conceptualizations of the pain-PTSD link. For more information on this topic, the interested reader is referred to reviews by Sharp and Harvey [82], Beck and Clapp [79], as well as Brennstuhl, Tarquinio, and Montel [83]. The pain-PTSD link has been verified mainly within populations that are

particularly vulnerable to experiencing PTSD, such as war veterans [1] and individuals who lived through a major disaster such as a severe earthquake [84] or another often-traumatic life circumstance like becoming a refugee [85]. The latter authors noted that chronic pain is extremely common in their target population and that it is likely to maintain the mental symptoms of trauma. More research is needed on the pain-PTSD link within the general population of older adults.

Anxiety and perception of pain

According to Sharp and Harvey [82], the relationship between anxiety and PTSD serves an important role in heightening the perception of pain among individuals with comorbid PTSD and pain. The aforementioned authors conceptualized pain perception as being enhanced by anxiety while maximizing the level of pain sensed, emotional discomfort, and physical impairments. Some studies have supported this claim, such as research on patients with accident-related chronic pain [86].

Upon using neuroimaging to capture neural structures associated with pain processing in individuals with PTSD within a sample of veterans who had experienced combat and veterans who had not, following the administration of a fixed-temperature assessment, it was discovered that perception of pain was reduced among individuals with PTSD [87]. Neuroimaging reports also showed specific patterns of activity within neural structures, such as increased activity within the left hippocampal region and reduced activity within the bilateral ventrolateral prefrontal cortex and the right amygdala during the fixed-temperature assessment among individuals with PTSD. Neuroimaging conducted during the individual temperature assessment indicated an increase in activity within the right putamen and bilateral insula, as well as reduced activity within the right precentral gyrus and right amygdala. This study's authors hypothesized that the unique patterns of activity within these neural structures contribute to the difference in processing pain among individuals with PTSD [87].

Some scholars have contended that anxiety is a potential determinant of comorbid pain and PTSD [79]. Indeed, there is empirical support for a significant role of anxiety in both increased pain sensitivity and PTSD, based on research findings on a sample of burn victims studied over the course of one year following the traumatic injury. Variables including the anxiety and dissociation that developed within a year's span of the onset of the trauma, as well as female gender, were significant predictors of PTSD [88]. The results of this investigation suggest that anxiety may play an essential role in the development of comorbid pain and PTSD.

Anxiety sensitivity

The conceptualization of anxiety sensitivity is based upon the mutual maintenance model of Sharp and Harvey [82]. It includes elements that contribute to perpetuating the comorbidity of PTSD and chronic pain, recognizing that individuals with comorbid PTSD and pain share a discomfort with arousal-based sensations [89]. The foundation of the anxiety sensitivity mechanism is the misperception of all anxious sensations as dangerous; thus, individuals with comorbid PTSD and pain may be more inclined to inaccurately perceive and unconsciously exaggerate physical sensations such as pain and arousal [90,91]. In a male veteran sample, research findings confirmed the mediating role of anxiety sensitivity in the maintenance of comorbidity between PTSD and chronic pain [92]. These results are similar to more recent empirical findings [93] on chronic musculoskeletal pain patients of an unspecified age residing in Spain.

Vulnerability model

Asmundson, Coons, Taylor, and Katz [94] used features of Sharp and Harvey's conceptualization of anxiety sensitivity [82] to develop the vulnerability model. They suggested that anxiety sensitivity is a variable present prior to the experience of trauma or pain and is a predisposing factor in the development of PTSD and chronic pain. Asumundson et al.'s model proposes that anxiety sensitivity functions as a foundation for an enhanced awareness of danger during traumatic experiences, affecting sensitivity to both mental and physical distress [94]. This sensitivity contributes to the development of comorbid PTSD and pain conditions. Empirical evidence is lacking on this theory.

Avoidant coping

Avoidant coping has been explored in the literature regarding pain and PTSD independently. Foa, Steketee, and Rothbaum [95] proposed that the development of presenting symptoms associated with PTSD is explained by the cognitive structure of fear (by Lang [96]). Lang's classic conceptualization of fear includes three aspects: 1) the feared stimuli, 2) somatic reactions and physical movement, as well as 3) the perception of the feared stimuli. The trauma-related memories formed based on these three variables influence the development of an automatic motive for escape from the perceived threatening stimuli. Lang described the process of developing a constant motive for escape from specific stimuli as being "programmed" to escape, based on the formulated structure of fear regarding the traumatic stimuli. Foa et al. hypothesized that stimuli in the environment may arouse the cognitive structure of fear and provoke behaviors of escape or avoidance from the feared stimuli [95]. As a result, the lack of exposure to the feared stimuli may result in an inability to extinguish the fear and develop more comfort and reassurance of safety in the presence of the stimuli, maintaining the symptoms of PTSD. Vlaeyen and Linton [97] conceptualized pain-related fear as prompting avoidant behaviors in regard to physical activity and as a core element in the development of chronic pain from a previously acute condition, leading to a pain-related disability. Avoidant coping behaviors contribute to both the maintenance and the development of PTSD and chronic pain conditions, and can potentially contribute to their comorbidity [98].

Attentional bias

Williams, Mathews, and MacLeod defined attentional bias as a reaction to a stimulus that may be deferred [99]. The Stroop task is an example of the effect of attentional bias on activity, as the task examines the effect of interference on speed of reaction. Stroop originally assessed color as a variable of interference on an individual's reaction time. Specifically, the task requires the individual to name the color of the ink and not read the word. For instance, if the word "GREEN" is in blue ink, the individual must state the word "blue." Stroop found that reaction time was longer and included many more errors when words did not match the color in which they were written than when both word and color of the text matched [100]. Support for the attentional bias is displayed in individuals who may have an increased delay in identifying the color of the word related to their pathology as opposed to neutral words [79]. Scholars have extended this conceptualization to cover delays in recognizing words related to pain among individuals with chronic pain [101].

In a study pertinent to the chronic pain-PTSD link, researchers observed an attentional bias within individuals experiencing both conditions in a sample of motor vehicle accident survivors, who were categorized into groups of those who had comorbid PTSD and chronic pain, only chronic pain, and a control group without PTSD or chronic pain. Some stimulus words were related to trauma, some to pain, some were neutral words, and some were positive words. Responses made by individuals with comorbid PTSD and chronic pain were delayed for both trauma and pain words, while individuals with only pain experienced delays only when presented with words related to pain [102]. These results are indicative of the critical role that attentional bias has in relation to comorbid pain and PTSD, given the interplay between PTSD and chronic pain in attentional processing [79]. Research is needed to provide explanations of the possible relationship between pain and PTSD in the context of attentional bias.

Table 1: Summary of Main Findings

Topic	Research Population	Main Findings/Theory	Citation
A. Potential Explanations of Comorbidity of Depression and Pain	1. Individuals with comorbid chronic pain and depression	1. a. The source of depression in individuals with chronic pain is a predisposition to depression that results from the stress of the pain condition b. Responses of medical practitioners to individuals' experience of chronic pain may be perceived as dismissing and serve as a stressor in the development of depression	1. a and b. Banks and Kerns [35]
	2. Individuals with comorbid depression, fibromyalgia, and neuropathic pain	2. a. Brain abnormalities may lead to a bidirectional relationship between chronic pain and depression b. Overstimulation of the HPA axis due to exposure to stressor(s) over a continuous period of time may impair HPA axis and influence cortisol levels, resulting in experience of pain and disruption of mood	2. a. Maletic and Riason [37] b1. Aguglia, Salvi, Maina, Rossetto, Aguglia [60] b2. Gracely, Ceko, Bushnell [61]
	3. a. Premenopausal women with chronic pain and depression b. Older adults c. Individuals with fibromyalgia	3. An abundance of pro-inflammatory proteins may be involved in the comorbidity of pain and depression	3. a. Hartman et al. [63] b. Penninx et al. [69] c. Gür, Karakoç, Nas, Denli, & Saraç [72]
B. Potential Explanations of Comorbidity of PTSD and Pain -	1. Patients with accident-related chronic pain 2. Veterans with PTSD who had experienced combat versus veterans who had not 3. a. Burn victims b. Veterans c. Chronic musculoskeletal pain patients 4. No population tested 5. a. Individuals with PTSD symptomatology b. Individuals with musculoskeletal pain c. Individuals with comorbid PTSD and chronic pain 6. a. Individuals with chronic pain b. Motor vehicle accident survivors with comorbid PTSD and chronic pain or with only chronic pain	1. Anxiety enhances the perception of pain 2. Pain is processed differently among individuals with PTSD 3. Sensitivity to anxious or arousal-based stimuli can contribute to the development and maintenance of comorbid PTSD and pain 4. Anxiety sensitivity for an enhanced awareness of danger during trauma may contribute to developing comorbid PTSD and chronic pain conditions 5. a. The use of avoidant coping to deal with fearful stimuli and consequent inability to extinguish the fear maintain symptoms of PTSD b. Acute pain may develop into a chronic pain-related disability as a result of pain-related fear and avoidant behaviors c. Avoidant coping behaviors can contribute to the maintenance and development of comorbid PTSD and pain 6. a. Delayed recognition of words related to pain b. Delayed recognition of words related to both pain and trauma among individuals with PTSD and chronic pain; delayed recognition of words related only to pain among those with only chronic pain	1. Geisser, Roth, Bachman, and Eckert [86] 2. Gueze et al. [87] 3. a. Van Loey, Maas, Faber, & Taal [88] b. Jakupcak et al. [92] c. López-Martínez, Ramírez-Maestre, and Esteve [93] 4. Asmundson, Coons, Taylor, & Katz [94] 5. a. Foa, Steketee, & Rothbaum [95] b. Vlaeyen and Linton [97] c. Bosco, Gallinati, & Clark [98] 6. a. Pincus & Morley [101] b. Beck, Freeman, Shipherd, Hamblen, & Lackner [102]
C. Potential Explanation of Comorbidity of Depression, PTSD, and Pain	1. Older adults with widespread pain 2. a. and b. Male veterans c. Individuals with chronic pain as a result of an accident 3. Women with depression and women with PTSD	1. Evidence on the significance of the depression-PTSD-pain link 2. a. and b. Depression mediates the PTSD-pain link c. PTSD is directly related to depression; depression is directly related to pain magnitude and indirectly to pain intensity via its effect on disability 3. Depression, PTSD, and vulvodynia may share patho-physiological patterns and risk factors	1. Häuser, Glaesmer, Schmutzer, & Brähler [103] 2. a. Jakupcak et al. [92] b. Poundja, Fikretoglu, & Brunet [104] c. Roth, Geisser, & Bates [105] 3. Iglesias-Rios, Harlow, & Reed [106]

A Potential Explanation of Comorbidity of Depression, PTSD, Pain and a Brief Review of Pertinent Research

Depression and decreased behavioral activity

The depression and decreased behavioral activity is a straightforward conceptualization that incorporates both PTSD and depression in relation to pain. As postulated by Sharp and Harvey [82], it presupposes that both PTSD and chronic pain could be maintained by fatigue and lethargy and by the often-related reduction in activity levels. At the present time, few researchers have studied these three variables simultaneously, and even fewer have targeted older adults specifically. In this regard, a Web of Science database search using the terms "older adults pain depression PTSD" did not return any relevant publication. However, the search "elderly pain depression PTSD" did yield one pertinent cross-sectional study sampled from the general German population aged 60 to 85, 19% of whom reported widespread pain [103]. Compared to control participants, older adults living with widespread pain had a higher prevalence of potential depressive disorder and PTSD.

Briefly, regarding non-geriatric research, studies focused on the pain-depression-PTSD link include cross-sectional research in which it was found that PTSD impacts reports of physical discomfort by male veterans via underlying depressive symptomatology and anxiety sensitivity [92]. In another study on male veterans, researchers discovered that the pain-PTSD link was fully mediated by depression [104]. Moreover, among individuals in chronic pain as a result of an

accident, while PTSD was directly related to depression, depression was directly related to the magnitude of pain and indirectly related to pain intensity via its effect on disability [105]. In baseline data on 250 Veterans Affairs primary care patients, depression and PTSD were independently and significantly related to higher pain reports, as well as to higher rates of disability and lower quality of life [1]. As to relevant studies targeting women in particular, 2015 research showed that depressed women and women who screened positive for PTSD had a higher prevalence of having the pain disorder vulvodynia, which is indicative of the fact that 1) those two disorders can contribute to the probability of experiencing vulvodynia, or 2) as the study's authors pointed out, depression, PTSD, and vulvodynia share patho-physiological as well as risk profiles [106]. Table 1 offers a concise summary of the review provided herein.

Conclusions

There are numerous conceptualizations linking pain to depression or to PTSD, yet not enough explanations have been provided for the pain-depression-PTSD link. According to some of the aforementioned researchers, pain, depression, and PTSD are likely to share some common foundations in terms of physiological, neurological, and/or immunological mechanisms. Their interrelation is complex and needs to be further studied. As recommended by Outcalt and colleagues [1], clinicians should assess and treat both depression and PTSD in patients living with chronic pain. Interested researchers should adopt longitudinal designs, as most of the published information in this area is cross-sectional evidence and some of it is still merely speculative. The causality of the chronic pain-psychopathology link typically differs depending on each mental disorder and is often mediated by biological and psychosocial factors [107]. Scholars should investigate this topic with samples of older adults, also due to the fact that some of those factors could be age-dependent.

As already mentioned, despite the importance of investigating older adults' physical pain and its comorbidity with depression and PTSD symptomatology, most of the studies in this area are specific to war veterans who have a PTSD diagnosis. For instance, in 2015 research, chronic face, head, and neck pain were significantly related to depression among war veterans living with PTSD [108]. It is critical to study these variables within war veteran populations, given that they are at high risk for chronic pain and related neuro-behavioral problems [109]. This is also the case for other vulnerable populations that are particularly at risk for PTSD such as traumatized refugees [85]. Nevertheless, it is important to examine pain, PTSD, and depression in community-dwelling older adults who have not undergone such extreme experiences yet must deal with pain, depression, and PTSD on a regular basis. Moreover, as noted by Gureje [107], because the evolution of the pain-psychopathology comorbidity seems to differ for men and women, geriatric research is needed on this topic. Gender-specific pain-psychopathology models should be developed and tested, to provide accurate and, if needed, differential assessment and treatment options for men and women and reduce possible gender disparities in this geriatric research area.

Furthermore, race/ethnicity-specific geriatric studies on pain and related psychopathology should be conducted, in view of research findings indicating racial/ethnic differences in experimental and clinical pain and function among older knee osteoarthritis patients [110]. These results suggest possible racial/ethnic differences in the somatosensory system and in patho-physiological mechanisms. Indeed, compared to Caucasians, older racial/ethnic minority individuals are facing even higher health disparities than their younger counterpart in receiving needed medical care such as prostate cancer treatment [111]. More efforts should be made to reduce race/ethnicity-related disparities in geriatric care. To this end, it is highly recommended that researchers pay particular attention to racial/ethnic diversity when gathering older adult samples for future research on the interplay of the variables discussed in the present article. This will allow scholars to begin filling cultural research gaps on the pain-depression-PTSD link while accounting for important yet under-studied potential risk factors for pain such as the aforementioned perceived racial discrimination. In particular, it is critical to innovatively examine whether the results of existing empirical studies conducted primarily on Caucasian samples can be generalized to non-Caucasian older individuals. In turn, the findings of future studies may serve as foundations on which to base tailored pain assessment and management (including coverage of pain's psychiatric comorbidities) to be implemented in a culturally appropriate manner to reduce inequalities in health.

Acknowledgment

This research was supported by a grant from the National Institute of General Medical Sciences, award number 5SC3GM094075, Luciana Laganá, Principal Investigator. The content of this article does not necessarily represent the official views of the National Institute of General Medical Sciences and is solely the responsibility of the authors.

References

1. Outcalt SD, Kroenke K, Krebs EE, Chumbler NR, Wu J, et al. (2015) Chronic pain and comorbid mental health conditions: independent associations of posttraumatic stress disorder and depression with pain, disability, and quality of life. J Behav Med 38: 535-543.
2. National Institute on Aging (2007) Why population aging matters: A global perspective.
3. U.S. Census Bureau (1995) Sixty-five plus in the United States.
4. National Institute on Aging (2011) New disease patterns.
5. Wills J (2011) Vital Notes for Nurses: Promoting Health. Hoboken, New Jersey: John Wiley & Sons.
6. Penuel BK, Statler M, Hagen R (2013) Encyclopedia of Crisis Management.
7. World Health Organization (2013) Mental health and older adults.
8. Piette JD, Heisler M, Krein S, Kerr EA (2005) The role of patient-physician trust in moderating medication nonadherence due to cost pressures. Arch Intern Med 165: 1749-1755.
9. Lee S, Tsang A, Huang YQ, Zhang MY, Liu ZR, et al. (2007) Arthritis and physical-mental comorbidity in metropolitan China. J Psychosom Res 63: 1-7.
10. Hestbaek L, Leboeuf-Yde C, Kyvik KO (2006) Is comorbidity in adolescence a predictor for adult low back pain? A prospective study of a young population. BMC Musculoskelet Disord 7: 29.
11. Daar AS, Singer PA, Persad DL, Pramming SK, Matthews DR, et al. (2007) Grand challenges in chronic non-communicable diseases. Nature 450: 494-496.
12. Badley EM, Tennant A (1992) Changing profile of joint disorders with age: findings from a postal survey of the population of Calderdale, West Yorkshire, United Kingdom. Ann Rheum Dis 51: 366-371.
13. Kaye AD, Baluch A, Scott JT (2010) Pain management in the elderly population: a review. Ochsner J 10: 179-187.
14. Cavalieri TA (2007) Managing pain in geriatric patients. J Am Osteopath Assoc 107: 10-16.
15. Ferrell BA, Ferrell BR, Osterweil D (1990) Pain in the nursing home. J Am Geriatr Soc 38: 409-414.
16. Lapane KL, Quilliam BJ, Chow W, Kim MS (2013) Pharmacologic management of non-cancer pain among nursing home residents. J Pain Symptom Manage 45: 33-42.
17. Mann J, Shuster J, Moawad N (2013) Attributes and barriers to care of pelvic pain in university women. J Minim Invasive Gynecol 20: 811-818.
18. Jiang X, Sandberg ME, Saevarsdottir S, Klareskog L, Alfredsson L, et al. (2015) Higher education is associated with a better rheumatoid arthritis outcome concerning for pain and function but not disease activity: results from the EIRA cohort and Swedish rheumatology register. Arthritis Res Ther 17: 317.
19. McIlvane JM (2007) Disentangling the effects of race and SES on arthritis-related symptoms, coping, and well-being in African American and White women. Aging Ment Health 11: 556-569.
20. Burgess DJ, Grill J, Noorbaloochi S, Griffin JM, Ricards J, et al. (2009) The effect of perceived racial discrimination on bodily pain among older African American men. Pain Med 10: 1341-1352.
21. U.S. Department of Health and Human Services (2012) Results from 2012 national survey on drug use and health: Mental health findings.
22. Barry LC, Allore HG, Guo Z, Bruce ML, Gill TM (2008) Higher burden of depression among older women: the effect of onset, persistence, and mortality over time. Arch Gen Psychiatry 65: 172-178.

23. Blackburn-Munro G, Blackburn-Munro RE (2001) Chronic pain, chronic stress and depression: coincidence or consequence? J Neuroendocrinol 13: 1009-1023.

24. Bair MJ, Wu J, Damush TM, Sutherland JM, Kroenke K (2008) Association of depression and anxiety alone and in combination with chronic musculoskeletal pain in primary care patients. Psychosom Med 70: 890-897.

25. Arnow BA, Hunkeler EM, Blasey CM, Lee J, Constantino MJ, et al. (2006) Comorbid depression, chronic pain, and disability in primary care. Psychosom Med 68: 262-268.

26. Morley S, Williams AC, Black S (2002) A confirmatory factor analysis of the Beck Depression Inventory in chronic pain. Pain 99: 289-298.

27. Merskey H (1994) Classification of Chronic Pain: Descriptions of Chronic Pain Syndromes and Definitions of Pain Terms. (2nd edn), IASP Press.

28. Ruoff GE (1996) Depression in the patient with chronic pain. J Fam Pract 43: S25-33.

29. Dworkin RH, Gitlin MJ (1991) Clinical aspects of depression in chronic pain patients. Clin J Pain 7: 79-94.

30. Geerlings SW, Twisk JW, Beekman AT, Deeg DJ, van Tilburg W (2002) Longitudinal relationship between pain and depression in older adults: sex, age and physical disability. Soc Psychiatry Psychiatr Epidemiol 37: 23-30.

31. Kiefer MM, Chong C (2014) Pocket Primary Care.Philadelphia, Wolters Kluwer/Lippincott Williams & Wilkins Health.

32. Staud R, Rodriguez ME (2006) Mechanisms of disease: pain in fibromyalgia syndrome. Nat Clin Pract Rheumatol 2: 90-98.

33. Bair MJ, Robinson RL, Katon W, Kroenke K (2003) Depression and pain comorbidity: a literature review. Arch Intern Med 163: 2433-2445.

34. Brooks A, Kominek C, Pham TC, Fudin J (2016) Exploring the Use of Chronic Opioid Therapy for Chronic Pain: When, How, and for Whom? Med Clin North Am 100: 81-102.

35. Banks SM, Kerns RD (1996) Explaining high rates of depression in chronic pain: A diathesis-stress framework. Psychol Bull 119: 95-110.

36. Richards SC, O'Hara MW (2014) The Oxford Handbook of Depression and Comorbidity.

37. Maletic V, Raison CL (2009) Neurobiology of depression, fibromyalgia and neuropathic pain. Front Biosci (Landmark Ed) 14: 5291-5338.

38. Neugebauer V, Li W, Bird GC, Han JS (2004) The amygdala and persistent pain. Neuroscientist 10: 221-234.

39. Rainville P, Bao QV, Chrétien P (2005) Pain-related emotions modulate experimental pain perception and autonomic responses. Pain 118: 306-318.

40. Apkarian AV, Sosa Y, Sonty S, Levy RM, Harden RN, et al. (2004) Chronic back pain is associated with decreased prefrontal and thalamic gray matter density. J Neurosci 24: 10410-10415.

41. Fitzgerald PB, Laird AR, Maller J, Daskalakis ZJ (2008) A meta-analytic study of changes in brain activation in depression. Hum Brain Mapp 29: 683-695.

42. Frodl TS, Koutsouleris N, Bottlender R, Born C, Jäger M, et al. (2008) Depression-related variation in brain morphology over 3 years: effects of stress? Arch Gen Psychiatry 65: 1156-1165.

43. Wiech K, Ploner M, Tracey I (2008) Neurocognitive aspects of pain perception. Trends Cogn Sci 12: 306-313.

44. Borsook D, Becerra L, Carlezon WA Jr, Shaw M, Renshaw P, et al. (2007) Reward-aversion circuitry in analgesia and pain: implications for psychiatric disorders. Eur J Pain 11: 7-20.

45. Drevets WC, Price JL, Furey ML (2008) Brain structural and functional abnormalities in mood disorders: implications for neurocircuitry models of depression. Brain Struct Funct 213: 93-118.

46. Goto Y, Grace AA (2005) Dopaminergic modulation of limbic and cortical drive of nucleus accumbens in goal-directed behavior. Nat Neurosci 8: 805-812.

47. Epstein J, Pan H, Kocsis JH, Yang Y, Butler T, et al. (2006) Lack of ventral striatal response to positive stimuli in depressed versus normal subjects. Am J Psychiatry 163: 1784-1790.

48. Wood PB, Schweinhardt P, Jaeger E, Dagher A, Hakyemez H, et al. (2007) Fibromyalgia patients show an abnormal dopamine response to pain. Eur J Neurosci 25: 3576-3582.

49. McClung CA, Nestler EJ (2008) Neuroplasticity mediated by altered gene expression. Neuropsychopharmacology 33: 3-17.

50. Bär KJ, Brehm S, Boettger MK, Boettger S, Wagner G, et al. (2005) Pain perception in major depression depends on pain modality. Pain 117: 97-103.

51. Graff-Guerrero A, Pellicer F, Mendoza-Espinosa Y, Martínez-Medina P, Romero-Romo J, et al. (2008) Cerebral blood flow changes associated with experimental pain stimulation in patients with major depression. J Affect Disord 107: 161-168.

52. Clauw DJ, Chrousos GP (1997) Chronic pain and fatigue syndromes: overlapping clinical and neuroendocrine features and potential pathogenic mechanisms. Neuroimmunomodulation 4: 134-153.

53. Crofford LJ, Young EA, Engleberg NC, Korszun A, Brucksch CB, et al. (2004) Basal circadian and pulsatile ACTH and cortisol secretion in patients with fibromyalgia and/or chronic fatigue syndrome. Brain Behav Immun 18: 314-325.

54. Dinan TG (2001) The hypothalamic-pituitary-adrenal axis in antidepressant action. In: Leonard BE, Antidepresssants. Basel: Birkhäuser, 83-94.

55. Korszun A (2002) Facial pain, depression and stress - connections and directions. J Oral Pathol Med 31: 615-619.

56. Tsigos C, Chrousos GP (2002) Hypothalamic-pituitary-adrenal axis, neuroendocrine factors and stress. J Psychosom Res 53: 865-871.

57. Coplan JD, Andrews MW, Rosenblum LA, Owens MJ, Friedman S, et al. (1996) Persistent elevations of cerebrospinal fluid concentrations of corticotropin-releasing factor in adult nonhuman primates exposed to early-life stressors: implications for the pathophysiology of mood and anxiety disorders. Proc Natl Acad Sci U S A 93: 1619-1623.

58. Contrada R, Baum A (2010) The Handbook of Stress Science: Biology, Psychology, and Health,Springer Publishing Company,704.

59. Talbott SM, Kraemer WJ (2007) The Cortisol Connection, Hunter House, 324.

60. Aguglia A, Salvi V, Maina G, Rossetto I, Aguglia E (2011) Fibromyalgia syndrome and depressive symptoms: comorbidity and clinical correlates. J Affect Disord 128: 262-266.

61. Gracely RH, Ceko M, Bushnell MC (2012) Fibromyalgia and depression. Pain Res Treat 2012: 486590.

62. Blackburn-Munro G (2004) Pain-like behaviours in animals - how human are they? Trends Pharmacol Sci 25: 299-305.

63. Hartman JM, Berger A, Baker K, Bolle J, Handel D, et al. (2006) Quality of life and pain in premenopausal women with major depressive disorder: the POWER Study. Health Qual Life Outcomes 4: 2.

64. National Institute of Neurological Disorders and Stroke (2010) Pain: hope through research.

65. Dinarello CA (2000) Proinflammatory cytokines.Chest 118: 503-508.

66. Strouse TB (2007) The relationship between cytokines and pain/depression: a review and current status. Curr Pain Headache Rep 11: 98-103.

67. Leonard BE (2001) The immune system, depression and the action of antidepressants. Prog Neuropsychopharmacol Biol Psychiatry 25: 767-780.

68. Ramamoorthy S, Ramamoorthy JD, Prasad PD, Bhat GK, Mahesh VB, et al. (1995) Regulation of the human serotonin transporter by interleukin-1 beta. Biochem Biophys Res Commun 216: 560-567.

69. Penninx BW, Kritchevsky SB, Yaffe K, Newman AB, Simonsick EM, et al. (2003) Inflammatory markers and depressed mood in older persons: results from the Health, Aging and Body Composition study. Biol Psychiatry 54: 566-572.

70. National Center for Biotechnology Information (2001) Neuroglial Cells.

71. Watkins LR, Maier SF (2005) Immune regulation of central nervous system functions: from sickness responses to pathological pain. J Intern Med 257: 139-155.

72. Gür A, Karakoç M, Nas K, Remzi, Cevik, et al. (2002) Cytokines and depression in cases with fibromyalgia. J Rheumatol 29: 358-361.

73. Acierno R, Lawyer SR, Rheingold A, Kilpatrick DG, Resnick HS, et al. (2007) Current psychopathology in previously assaulted older adults. J Interpers Violence 22: 250-258.

74. van Zelst WH, de Beurs E, Beekman AT, Deeg DJ, van Dyck R (2003) Prevalence and risk factors of posttraumatic stress disorder in older adults. Psychother Psychosom 72: 333-342.

75. Breslau N, Kessler RC (2001) The stressor criterion in DSM-IV posttraumatic stress disorder: an empirical investigation. Biol Psychiatry 50: 699-704.

76. Kessler RC, Sonnega A, Bromet E, Hughes M, Nelson CB (1995) Posttraumatic stress disorder in the National Comorbidity Survey. Arch Gen Psychiatry 52: 1048-1060.

77. Perkonigg A, Kessler RC, Storz S, Wittchen H -U (2000) Traumatic events and post-traumatic stress disorder in the community: prevalence, risk factors and comorbidity. Acta Psychiatr Scand 101: 46-59.

78. Tolin DF, Foa EB (2002) Gender and PTSD: A cognitive model. In: R Kimerling, P Ouimette, J Wolfe, Gender and PTSD, 76-97, New York,The Guilford Press.

79. Beck JG, Clapp JD (2011) A different kind of co-morbidity: Understanding posttraumatic stress disorder and chronic pain. Psychol Trauma 3: 101-108.

80. Von Korff M, Crane P, Lane M, Miglioretti DL, Simon G, et al. (2005) Chronic spinal pain and physical-mental comorbidity in the United States: results from the national comorbidity survey replication. Pain 113: 331-339.

81. Sareen J, Cox BJ, Stein MB, Afifi TO, Fleet C, et al. (2007) Physical and mental comorbidity, disability, and suicidal behavior associated with post traumatic stress disorder in a large community sample. Psychosom Med 26: 242-248.

82. Sharp TJ, Harvey AG (2001) Chronic pain and posttraumatic stress disorder: mutual maintenance? Clin Psychol Rev 21: 857-877.

83. Brennstuhl MJ, Tarquinio C, Montel S (2015) Chronic Pain and PTSD: Evolving Views on Their Comorbidity. Perspect Psychiatr Care 51: 295-304.

84. Ozdemir O, Boysan M, Guzel Ozdemir P, Yilmaz E (2015) Relationships between posttraumatic stress disorder (PTSD), dissociation, quality of life, hopelessness, and suicidal ideation among earthquake survivors. Psychiatry Res 228: 598-605.

85. Nordbrandt MS, Carlsson J, Lindberg LG, Sandahl H, Mortensen EL (2015) Treatment of traumatised refugees with basic body awareness therapy versus mixed physical activity as add-on treatment: Study protocol of a randomised controlled trial. Trials 16: 477.

86. Geisser ME, Roth RS, Bachman JE, Eckert TA (1996) The relationship between symptoms of post-traumatic stress disorder and pain, affective disturbance and disability among patients with accident and non-accident related pain. Pain 66: 207-214.

87. Geuze E, Westenberg HG, Jochims A, de Kloet CS, Bohus M, et al. (2007) Altered pain processing in veterans with posttraumatic stress disorder. Arch Gen Psychiatry 64: 76-85.

88. Van Loey NE, Maas CJ, Faber AW, Taal LA (2003) Predictors of chronic posttraumatic stress symptoms following burn injury: results of a longitudinal study. J Trauma Stress 16: 361-369.

89. Reiss S, McNally RJ (1985) Expectancy model of fear. In: S Reiss, RR Bootzin, Theoretical issues in behavior therapy. New York: Academic Press, 107-121.

90. McFarlane AC, Atchison M, Rafalowicz E, Papay P (1994) Physical symptoms in post-traumatic stress disorder. J Psychosom Res 38: 715-726.

91. Crombez G, Eccleston C, Baeyens F, Eelen P (1998) When somatic information threatens, catastrophic thinking enhances attentional interference. Pain 75: 187-198.

92. Jakupcak M, Osborne T, Michael S, Cook J, Albrizio P, et al. (2006) Anxiety sensitivity and depression: mechanisms for understanding somatic complaints in veterans with posttraumatic stress disorder. J Trauma Stress 19: 471-479.

93. López-Martínez AE, Ramírez-Maestre C, Esteve R (2014) An examination of the structural link between post-traumatic stress symptoms and chronic pain in the framework of fear-avoidance models. Eur J Pain 18: 1129-1138.

94. Asmundson GJ, Coons MJ, Taylor S, Katz J (2002) PTSD and the experience of pain: research and clinical implications of shared vulnerability and mutual maintenance models. Can J Psychiatry 47: 930-937.

95. Foa EB, Steketee G, Rothbaum BO (1989) Behavioral/cognitive conceptualization of post-traumatic stress disorder. Behav Ther 20: 155-176.

96. Lang PJ (1977) Imagery in therapy: An information processing analysis of fear. Behav Ther 8: 862-886.

97. Vlaeyen JW, Linton SJ (2000) Fear-avoidance and its consequences in chronic musculoskeletal pain: a state of the art. Pain 85: 317-332.

98. Bosco MA, Gallinati JL, Clark ME (2013) Conceptualizing and Treating Comorbid Chronic Pain and PTSD. Pain Res Treat 2013: 174728.

99. Williams JM, Mathews A, MacLeod C (1996) The emotional Stroop task and psychopathology. Psychol Bull 120: 3-24.

100. Stroop JR (1935) Studies of interference in serial verbal reactions. J Exp Psychol 18: 643-662.

101. Pincus T, Morley S (2001) Cognitive-processing bias in chronic pain: a review and integration. Psychol Bull 127: 599-617.

102. Beck JG, Freeman JB, Shipherd JC, Hamblen JL, Lackner JM (2001) Specificity of Stroop interference in patients with pain and PTSD. J Abnorm Psychol 110: 536-543.

103. Häuser W, Glaesmer H, Schmutzer G, Brähler E (2012) Widespread pain in older Germans is associated with posttraumatic stress disorder and lifetime employment status--results of a cross-sectional survey with a representative population sample. Pain 153: 2466-2472.

104. Poundja J, Fikretoglu D, Brunet A (2006) The co-occurrence of posttraumatic stress disorder symptoms and pain: is depression a mediator? J Trauma Stress 19: 747-751.

105. Roth RS, Geisser ME, Bates R (2008) The relation of post-traumatic stress symptoms to depression and pain in patients with accident-related chronic pain. J Pain 9: 588-596.

106. Iglesias-Rios L, Harlow SD, Reed BD (2015) Depression and Posttraumatic Stress Disorder among Women with Vulvodynia: Evidence from the Population-Based Woman to Woman Health Study. J Womens Health (Larchmt) 24: 557-562.

107. Gureje O (2007) Psychiatric aspects of pain. Curr Opin Psychiatry 20: 42-46.

108. Muhvić-Urek M, Vukšić Ž, Simonić-Kocijan S, Braut V, Braut A, et al. (2015) Co-Occurrence Of Chronic Head, Face And Neck Pain, And Depression In War Veterans With Post-Traumatic Stress Disorder. Acta Clin Croat 54: 266-271.

109. Cook AJ, Meyer EC, Evans LD, Vowles KE, Klocek JW, et al. (2015) Chronic pain acceptance incrementally predicts disability in polytrauma-exposed veterans at baseline and 1-year follow-up. Behav Res Ther 73: 25-32.

110. Cruz-Almeida Y, Sibille KT, Goodin BR, Petrov ME, Bartley EJ, et al. (2014). Racial and ethnic differences in older adults with knee osteoarthritis. Arthritis Rheumatol 66: 1800-1810.

111. Mahal BA, Ziehr DR, Aizer AA, Hyatt AS, Lago-Hernandez C, et al. (2014) Racial disparities in an aging population: the relationship between age and race in the management of African American men with high-risk prostate cancer. J Geriatr Oncol 5: 352-358.