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Exploring the Role of Insomnia in the Relation between PTSD and Pain in Veterans with Polytrauma Injuries

Katie Patricia Lang

EXPLORING THE ROLE OF INSOMNIA IN THE RELATION BETWEEN PTSD AND PAIN IN VETERANS WITH POLYTRAUMA INJURIES

by

Katie Patricia Lang

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ABSTRACT

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Soldiers returning from Operation Enduring (OEF) and Iraqi (OIF) Freedom endure many polytrauma injuries including traumatic brain injury (TBI). This study examines the role of insomnia, PTSD and pain-related outcomes in a sample of TBI veterans. The medical records of 147 OEF/OIF veterans seen at a VAMC Polytrauma clinic were reviewed. Analyses indicated a high prevalence of PTSD, insomnia, and pain in this population, co-occurring in 47.6% of veterans. Increased PTSD symptomatology was significantly correlated with reports of more pain severity (r = .51), pain interference (r = .56), and insomnia (r = .64). Insomnia partially mediated the relation between PTSD and both pain severity and interference. These results indicate the overlap and complexity of presenting complaints in OEF/OIF veterans and highlight the role of sleep disturbances in complicating diagnosis and treatment of veterans. They further suggest the importance of a multidisciplinary team approach to assessing and treating these veterans.

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CHAPTER 1

INTRODUCTION

Due to innovations in military protective equipment and medical care surrounding the military efforts of Operation Enduring Freedom (OEF) and Iraqi Freedom (OIF), soldiers are experiencing an increased survival rate. The Department of Defense reports that the percentage of death due to combat injuries has decreased from 30% during World War II and 24% in Vietnam to just 10% of soldiers from OEF/OIF (Gawande, 2004). In addition to improved medical care, the increased usage of imprecise weapons like improvised explosive devices (IEDs) has impacted this reduction in lethality of injuries. This new type of warfare is leaving veterans alive, but with a complex constellation of polytrauma injuries. In 2005 the Veterans Health Administration defined polytrauma as "injury to the brain in addition to other body parts or systems resulting in physical, cognitive, psychological, or psychosocial impairments and functional disability" (VHA, 2005). Recent research has suggested that the high rates of traumatic brain injury (TBI), pain, and posttraumatic stress disorder (PTSD), which make up the "polytrauma clinical triad," have been concurrently diagnosed in as many as 42% of OEF/OIF veterans (Lew et al., 2009). Additionally, each condition comprising the polytrauma triad is independently associated with other psychosocial factors, such as sleep disturbances that complicate accurate diagnosis and effective treatment of veterans.

Traumatic Brain Injury

Traumatic brain injury is a physical injury to the brain caused by blows or jolts to the head that can range in severity from mild to severe. Mild TBI (mTBI) is the most common type of TBI and accounts for an estimated 75% of all brain injuries in both

civilian and military populations (Centers for Disease Control and Prevention, 2003). It is estimated that as many as 13% of soldiers deployed with OEF/OIF report a closed brain injury consistent with a mTBI (MacGregor et al., 2010). The most common cause of this type of brain injury is exposure to a blast from an IED or other explosive device (Hoge et al., 2008; Okie, 2005; Warden, 2006). A blast creates a sudden increase in air pressure by heating and accelerating air molecules and, immediately thereafter, a sudden decrease in pressure that produces intense wind (Okie, 2005). In this situation, damage to the brain can occur from either the impact of the blast waves themselves, the force of an object from the blast, or the impact of the brain striking against the skull (Okie, 2005; Warden, 2006). IED explosions typically result in a combination of mechanical injury with primary blast wave (e.g., a veteran is in a vehicle that encounters an IED, and is subject both to the explosion and injuries incurred from hitting the interior panels of the vehicle) (Warden, 2006). Because of the sudden and violent nature of brain injury via blast exposure, concurrent and subsequent psychological trauma often occurs in addition to the physical injury (Kennedy, Leal, Lewis, Cullen, & Amador, 2010).

Symptoms characterizing mTBI include physical (e.g., headaches, dizziness, insomnia), cognitive (e.g., impaired attention, memory, executive functioning), emotional (e.g., depression, anxiety, irritability), and behavioral (e.g., impulsivity, aggression) impairments (Rao & Lyketsos, 2000). Although the majority of patients with mild brain injury will experience at least some of these symptoms immediately post-injury (Levin et al., 1987), the majority of individuals experience complete symptom resolution within a year post injury (McAllister, 2009; Okie, 2005). Of those patients who continue to

experience symptoms past 6 months, the primary complaints include dizziness, headache, and fatigue (McCullagh, Oucherlony, Protzner, Blair, & Feinstein, 2001).

The dynamics underlying impairment due to brain injury are not yet fully understood. For example, it is unclear whether brain injury incurred via a blast mechanism leads to different sequelae than that caused by a non-blast (Belanger, Kretzmer, Yoash-Gantz, Pickett, & Tupler, 2009). It is likely that both blast and non-blast TBI results in equivalent severity of stress symptoms but that the rate of psychiatric disturbances, particularly PTSD, following blast-related TBI is higher than following other types of brain injury (Kennedy et al., 2010; Warden, 2006). One significant physical sequela of TBI is chronic pain, particularly headache pain. Although the prevalence rate of pain varies widely in the literature, a systematic of pain in polytrauma patients found that headache was the most common type of pain among TBI patients (Dobscha et al., 2009), likely affecting as many as 58% of TBI patients (Nampiaparampil, 2008). With the increasing number of service members returning from OEF/OIF who have experienced TBI it is of mounting importance that the psychosocial consequences of this type of injury continue to be researched to optimize health care.

Pain

Pain is a subjective experience with sensory, emotional, cognitive, and sociocultural components (Kemperman et al., 1997), and can be experienced in a variety of ways. Henry Beecher (1959) was among the first to explain the dimensionality of pain, which he theorized when treating WWII veterans and regular medical patients. The two dimensions that Beecher pioneered are widely recognized as sensory (e.g., intensity, location, quality), and reactive (e.g., emotional reaction to pain, fears and concerns about

pain). Subsequent researchers have labeled these constructs "sensory-discriminative" and "attitudinal" (Clark & Yang, 1983), while others have focused on dimensions of motivational-affective and cognitive-evaluative (Melzack & Casey, 1968). Despite the variation in names, what is apparent is that pain is experienced by its physical intensity and also by its cognitive interference with daily life. Despite the recognized dimensions of pain, researchers often focus only on the intensity of pain (Andrasik, Blanchard, Ahles, Pallmeyer, & Barron, 1981) leaving out the cognitive aspect of pain interference. This omission could impact the accuracy of diagnosis and result in an inadequate treatment plan.

Pain is a nearly universal consequence of polytrauma and is a very common sequela of brain injury. Despite inconsistencies in the literature, it is expected that up to 95% of veterans who suffer a TBI will experience chronic pain (Sayer et al., 2008). Chronic pain is referred to as pain that persists for longer than 3 months, that initially accompanies a disease process or bodily injury that may have resolved or healed (ISAP, 1994). Not surprisingly, chronic pain often interferes with occupational, social, and recreational activities in veterans and contributes to poor rehabilitation outcomes (Otis et al., 2010).

Recent research has suggested possible risk factors of increased pain in OEF/OIF veterans. A recent systematic review by Nampiaparampil (2008) found that 51% of patients with mTBI reported chronic pain compared to only 32% of patients with moderate or severe TBI, suggesting that pain may vary with severity of TBI. Additionally, mental health concerns, such as PTSD and depression, are often present with chronic pain and result in more intense pain, affective distress, life interference, and

disability (Andrasik, 2009). What is clear is that pain affects a large percentage of veterans, particularly those who have experienced polytrauma. For those veterans pain can be a complicating and chronic issue that is still not well understood in terms of integrative treatment.

Posttraumatic Stress Disorder

Posttraumatic stress disorder (PTSD) is an anxiety disorder characterized by three clusters of symptoms including reexperiencing of memories, either daytime memories and/or nightmares, avoidance of reminders, and hyperarousal symptoms such as increased irritability, and being overly vigilant. Although the majority of trauma victims do not develop a stress disorder, for those who do, PTSD can become a chronic condition that is associated with significant reductions in quality of life and functional impairments (Erbes, Westermeyer, Engdahl, & Johnsen, 2007). The lifetime incidence rate of PTSD is around 7%, making it the 5th most common psychological disorder in the USA (Kessler, Sonnega, Bromet, & Hughes, 1995). However, among military populations the prevalence is often higher, ranging from 8% of peacekeepers deployed to Somalia, to 19% of Gulf War veterans (Litz, Orsillo, Friedman, & Ehlich, 1997; Sutker, Uddo, Brailey, & Allain, 1993). A recent survey found that of all OEF/OIF veterans seen at VA health care facilities the most common mental health diagnosis was PTSD, which was diagnosed in 13-17% of veterans (Hoge et al., 2004; Seal, Bertenthal, Miner, Sen, & Marmar, 2007). However, among veterans reporting experiences consistent with mTBI, an estimated 40% screened positive for PTSD, which is roughly three times the rate in the absence of head trauma (Hoge et al., 2008).

Early researchers questioned whether PTSD could in fact occur as a result of TBI because the impaired or loss of consciousness that accompanies a brain injury conceptually would not permit processing of traumatic memories and fear conditioning. However, the high rate of comorbid PTSD and mTBI in military populations suggests that they must be able to co-occur. Recently, researchers demonstrated that implicit processing of traumatic memories and fear conditioning, both mechanisms for development of PTSD, actually can occur during brain injury (Hoge et al., 2008), yet there may be a reduced risk of developing PTSD following more severe brain injuries (Warden, 2006). However, for those individuals experiencing a mTBI it is likely that the violent and life-threatening circumstances associated with the injury are sufficient criteria for developing subsequent posttraumatic stress (Bryant, 2001; Jones, Young, & Leppma, 2010). Additionally, it is likely that the development of PTSD is often related to additional traumas that occur beyond the TBI incident and encompasses the entire combat experience.

Despite the elevated comorbidity between PTSD and brain injury, accurate diagnosis is difficult due to the high symptom overlap between the two conditions. Specifically, symptoms in each category of PTSD (reexperiencing, avoidance, and arousal) are also common in people suffering from TBI, including intrusive memories, social detachments, and insomnia (Bryant 2001). Additionally, chronic pain is another common overlapping symptom, affecting up to 66% of combat veterans with PTSD (Shipherd et al., 1997). One proposed reason accounting for the high comorbidity between PTSD and pain is an overlap of cognitive, affective and behavioral symptoms where PTSD maintains/exacerbates components of chronic pain and vice versa (Defrin et

al., 2008). This and several other theoretical models have been proposed (e.g., shared vulnerability) regarding the mechanisms underlying co-occurring pain and PTSD (Otis et al., 2003). However, there is a lack of empirical evidence to support any one theoretical model and further research is needed to investigate how other related conditions, like sleep disturbances, affect both pain and PTSD following combat.

Some evidence suggests that among veterans with TBI, those who are injured via blast report more reexperiencing symptoms of PTSD, particularly nightmares and flashbacks (Kennedy et al., 2010). This is consistent with similar findings that sleep disturbances in TBI veteran populations often co-occur with PTSD (Lew et al., 2010). Additional correlates relevant to the development of PTSD among veterans include substance use, depression, and anxiety (Feinstein, Hershkop, Jardine, & Ouchterlony, 2000). Taken together, the traumatic circumstances of combat often result in debilitating conditions for returning service members; however, only about one half of veterans screening positive for PTSD report utilizing some form of mental health service (Erbes et al., 2007). Further research is needed to evaluate the effectiveness of current treatments provided to veterans seeking care and also to understand how comorbid conditions of pain, sleep disturbances, and psychological conditions contribute to treatment for veterans exposed to mTBI.

Sleep Disturbances

Sleep disturbances are a core feature of PTSD, as evident by the inclusion of sleep symptoms in the diagnostic criteria for PTSD according to the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV-TR; APA, 2000). Typical self-reported sleep problems in this population include difficulty in sleep initiation and

maintenance, increased sleep onset latency, and increased number of awakenings (Lavie, Hefez, Halperin, & Enoch, 1979; Mikulincer, Glaubman, Wasserman, & Porat, 1989). Among combat veterans with PTSD, 44-90% report difficulties falling or staying asleep (Mellman, Kulick-Bell, Ashlock, & Nolan, 1995; Neylan et al., 1998), and 52-87% report having recurrent nightmares (Inman, Silver, & Doghramji, 1990; Neylan et al., 1998). Although subjective sleep disturbances are reported by a majority of individuals with PTSD, results from sleep laboratory studies using polysomnography are inconsistent in the ways that sleep architecture may be altered in patients with PTSD (Capaldi, Guerrero, & Killgore, 2011; Carskadon & Dement, 2000; Kobayshi, Boarts, & Delahanty, 2007; Yetkin, Aydin, & Ozgen, 2010).

Several recent studies have suggested that patients with PTSD experience more stage 1 sleep, greater REM density, longer sleep onset latency, less slow wave sleep, and less total sleep time (Kobayshi et al., 2007; Yetkin et al., 2010). A study comparing two different groups of patients with PTSD, those having this diagnosis alone versus those having comorbid major depressive disorder (MDD), to healthy controls found that patients in both PTSD groups had significantly more sleep disturbances than controls. Additionally, these disturbances were more prominent among those patients with comorbid MDD (Yetkin et al., 2010). Of particular interest is the finding that individuals with PTSD may experience less slow wave sleep, which is hypothesized to be restorative in humans (Carskadon & Dement, 2000). It is possible that the hyperarousal symptom cluster of PTSD has direct effects on sleep disturbances in veterans; the heightened state of arousal may make it difficult to fall asleep and also reduce sleep quality (Germain, Buysse, & Nofzinger, 2008). Although this link between PTSD and sleep disturbances is

logical, research surrounding the specific mechanisms underlying PTSD and sleep problems is limited.

Sleep disturbances, particularly insomnia, commonly co-occur with brain injury, and have been reported to be present in up to 84% of cases (Zeitzer, Friedman, & O'Hara, 2009). Despite the high prevalence, sleep symptoms have received limited scientific research. These symptoms are often minimized by patients relative to other TBI-related problems (e.g., cognitive, physical impairments). This is important considering that sleep problems can exacerbate other symptoms such as pain, cognitive deficits, fatigue, and irritability (Ouellet, Meaulieu-Bonneau, & Morin, 2006). Additionally, veterans with polytrauma injuries often experience high levels of stress, anxiety and feelings of hopelessness, all of which can heighten emotional or cognitive activity at bedtime and affect sleep quality (Ouellet & Beaulieu-Bonneau, 2011). Thus, when sleep disturbances are not addressed, it can compromise the overall rehabilitation of the individual.

In addition to PTSD and TBI, other risk factors for sleep disturbances include depression, fatigue, and pain (Lew et al., 2010; Ouellet et al., 2006; Zeitzer et al., 2009). One way that pain and sleep may interact is through the architecture of sleep (e.g., cyclical pattern of moving through the sleep stages) and its relation to pain sensitivity. For example, Hakkionen and colleagues (2001) compared the effects of sleep deprivation and sleep recovery on pain sensitivity in health adults. They found that sleep deprivation reduced pain thresholds and recovery of REM and slow wave sleep led to an increase in pain tolerance; however, the analgesic effect was greater in recovery of slow wave sleep. These results suggest that pain and sleep are interrelated and point to the need for further

research regarding the influence of other comorbid psychological conditions to inform effective treatment.

Purpose of Study

As military personnel continue to serve in Iraq and Afghanistan, the rate of veterans returning with polytrauma injuries is likely to remain a top concern for service providers. Common comorbid problems related to brain injury include PTSD, pain, and sleep disturbances. However, research addressing the interactions of such disorders with brain injury is still in its infancy. The aim of the present study was to explore what role sleep disorders, particularly insomnia, play in the relation between PTSD and pain-related outcomes in a sample of veterans with TBI. It is hypothesized that (1) PTSD, insomnia, pain severity, and pain interference will be significantly correlated with one another; (2) insomnia, pain severity, and pain interference will be significantly higher in veterans whose PTSD symptom severity is consistent with a diagnosis PTSD; and (3) insomnia will act as a partial mediating variable between PTSD and both pain-related outcomes. The outcome of this study may help refine the limited existing theoretical models attempting to link the three disorders, as well as improve the focus of clinical interventions and maximize treatment outcomes.

CHAPTER 2

METHOD

Participants and Procedures

The sample consisted of 147 U.S. military service members evaluated from November 2008 to January 2011 at a Veterans Affairs Medical Center (VAMC) in a large urban area in the Southern United States. Veterans in this study were initially screened as part of their post-deployment health evaluations mandated for all veterans of OEF/OIF. Those who were positive for potential TBI as measured by the four-item first level screen, a measure modified from the Brief Traumatic Brain Injury Screen (BTBIS; Schwab et al., 2006), continued to the second level screening in a Polytrauma clinic. As part of this screening, veterans complete various clinical measures. For the present study, data were obtained from a retrospective record review of veterans who had completed the second level Polytrauma screening. Data extracted from the Computerized Patient Record System (CPRS) database included patient demographic information and TBI status (judged by a clinician as either symptoms consistent with TBI, behavioral health conditions, a combination, or neither). This protocol was approved by the Memphis VAMC Institutional Review Board (IRB) and the University of Memphis IRB.

The sample was ethnically diverse with 52.4% of veterans self-reporting as White, 21.1% as African American, 15% as other; the remainder did not report race. Their median age was 30.7 years (range, 20 - 58) and the majority were male (95.1%). The majority of veterans served in the Army (48.6%). The others were in the National Guard (30.4%), Marines (10.1%), Air Force (4.1%), and Navy (2.7%). At the time of the TBI screen the majority of veterans were married (50.7%), 24.3% single, and 22.3% were

divorced or separated. Sixty one percent were unemployed or a current student, 30.4% employed full time, and 5.4% part time.

Measures

Posttraumatic Stress Disorder (PTSD) (see Appendix A). The PTSD Checklist-Civilian Version (PCL-C; Blanchard, Jones-Alexander, Buckley, & Forneris, 1996; Weathers, Litz, Huska, & Keane, 1993) is a 17-item self-report measure designed to assess PTSD symptomatology in areas of re-experiencing, avoidance and hyperarousal corresponding to criteria B, C, and D of the DSM-IV (APA, 2004). Using a 1 to 5 scale (1 = Not at All, 5 = Extremely), patients are asked to rate the extent to which they have been bothered by a problem in the past month (i.e., Trouble *remembering important* parts of a stressful experience from the past). Although scores range from 17 to 85, a cut-off score of 50 has been suggested to indicate clinically significant PTSD (Weathers et al., 1993). This measure is utilized as a continuous variable in the mediation model. Test-retest reliability for this scale is α = .96. Item 13, the question regarding difficulty falling or staying asleep, was eliminated from the summed score in order to decrease multicollinearity among measures and to more effectively delineate relationships among variables; reliability for this version of the measure is α = .96.

Sleep Disturbances (see Appendix B). The Insomnia Severity Index (ISI; Bastien, Vallieres, & Mortin, 2001) is a 7-item measure that asks participants to respond to potential behavioral and emotional aspects of insomnia (e.g., "Difficulty falling asleep," "How worried/distressed are you about your current sleep problem?") within the past two weeks. All items are scored from 0 to 4 (0 = not at all, 4 = extremely) and summed for a composite score with range of 0-28. Suggested ranges for interpretation are 0–7 no

clinically significant insomnia; 8–14 subthreshold insomnia; 15–21 clinical insomnia of moderate severity; 21–28 severe clinical insomnia (Smith & Wegener, 2003). Smith and Trinder (2001) found a cutoff score of 14 distinguished individuals with insomnia from those without with a sensitivity of 94% and specificity of 94%. This measure has shown adequate internal consistency (α = .74 - .78) and strong convergent validity between patient, clinician, and significant other's versions and with sleep diaries and polysomnographic measures (Bastien et al., 2001).

Pain (see Appendix C). To measure pain participants completed the Brief Pain Inventory- Short Form (BPI; Cleeland & Ryan, 1994), which assesses both pain severity and pain interference in the last 24 hours (both on a scale of 0 = No pain/ Interference to 10 = Pain as bad as bad as you can imagine/ Completely interferes). The pain severity subscale score is the mean of the 4 severity questions (pain at its worst, least, average, and now). The pain interference subscale score is the mean of the 7 interference questions (general activity, walking, work, mood, enjoyment of life, relations with others, and sleep). The first question ("Have you had pain other than everyday kinds of pain today?") was used as an inclusion rule in that participants who answered "no" were given a score of 0 for the severity and interference subscales. The BPI demonstrates high test-retest reliability and alternate-form reliability when pain is stable or when pain changes in a predictable way. The reliability for the pain severity subscale is α = .89. Item F, the item regarding the degree to which pain interferes with sleep, was eliminated from the pain interference subscale score in order to decrease multicollinearity among measures and to more effectively delineate relationships among variables; reliability for the 6-item pain interference subscale is α = .93.

Data Analysis

Participants who failed to answer any of the items on the PCLC measure (n = 1), the ISI measure (n = 1), the first 3 items of the ISI measure (n = 5), or the BPI severity measure (n = 4) were removed from the dataset. Missing data for the BPI interference were uncommon (both measures missing < 1% of data), and for those that were missing, an individual's item score was imputed using the participant average for the completed item (Downy & King, 1998). This data imputation allowed for 147 participants to be analyzed. All distributions were checked for outliers and skewness and kurtosis prior to analysis.

Our first hypothesis, that PTSD and insomnia are correlated with both pain severity and pain interference, was tested with Pearson bivariate correlations. Our second hypothesis, that pain severity, pain interference, and insomnia are significantly higher in veterans whose PTSD symptom severity is consistent with a diagnosis PTSD was tested with independent-samples t-tests. A dichotomous variable of PTSD status, as judged by the established cutoff score of 50 on the PCLC measure, was used as the grouping variable. Our third hypothesis, that veterans' severity of insomnia mediates the association between PTSD and the pain-related outcomes, was tested with multiple-linear regression analyses as suggested by Baron and Kenny (1986). This analysis was performed independently for each pain outcome (e.g., severity and interference).

The hypothesized mediation model indicates two causal paths leading to the dependent variable (pain): the direct effects of the independent variable (PTSD; *c*-path) and the mediator (insomnia; *b*-path). Additionally, there is a direct path from the independent variable (PTSD) to the mediator (insomnia; *a*-path). To test for mediation,

regression equations must first demonstrate a significant direct effect for both PTSD and insomnia on pain (*c*- and *b*-paths, respectively). Then, when both PTSD and insomnia are entered as predictors (*c'*-path) the indirect effect of PTSD on pain must be less than its direct effect (*c*-path). Complete mediation holds if PTSD has no effect on pain when controlling for insomnia (Baron & Kenny, 1986). Within social science research, partial mediation (*c*'-path < *c*-path) rather than complete mediation is more realistic because a single mediator cannot often be expected to completely explain the relation between an independent and dependent variable. Therefore, if PTSD still has an effect on pain when controlling for insomnia, partial mediation can be concluded if the reduction in strength from the *c*- to *c'*-path is significant (Baron & Kenny, 1986).

To test if the reduction in strength from the *c*-path to the *c'*-path is significant, the mediating effects of insomnia were verified with a bootstrapping method (with $n = 5000$ bootstrap resamples) to calculate the bias corrected confidence intervals (CI) around the mediated and direct effects. This was accomplished by employing the SPSS macros (Preacher & Hayes, 2008). Bootstrapping uses multiple samples, each containing *N* cases that are randomly drawn with replacement from the original sample, and the effects are then estimated for each bootstrap sample. These estimates are rank ordered by the bias-corrected bootstrapped CI to test the indirect effects. An indirect effect is significant if the CI does not contain zero. A 95% CI was used to assess mediation (Preacher & Hayes, 2004 & 2008). This procedure was conducted twice, using each pain subscale (severity and interference) separately as the criterion.

CHAPTER 3

RESULTS

Sample Characteristics

The correlations, means, and standard deviations among unadjusted study variables are displayed in Table 1. We conducted frequency analyses to determine the extent to which PTSD, insomnia, or pain was present in our sample, see Figure 2. Based on the PCLC cutoff score, 55.1% of veterans reported symptoms consistent with clinically significant PTSD. The majority of veterans (89%) reported some symptoms of insomnia with 66.6% of them scoring above the cutoff for clinically significant insomnia (Smith & Trinder, 2001). The majority of veterans (89%) reported experiencing pain other than everyday types of pain, as measured by the BPI, with 86% stating that their pain has interfered in some aspect of their lives. Additionally, 47.6% of veterans presented with a combination of PTSD, insomnia, and pain, and only 3.4% of the sample did not report any of these three conditions (see Figure 1). As predicted, veterans with higher scores on the PCLC measure, indicating stronger severity in PTSD symptoms, reported higher levels of pain severity and pain interference. Veterans with higher PCLC scores also reported experiencing more severe insomnia.

Table 1

Means, Standard Deviations (SD), and Correlations among Primary Study Variables

Study variables	2	3	4	*M*	*SD*
1.PTSD	.64**	.51**	.56**	53.53	17.52
2.Insomia		.58**	.59**	17.00	7.00
3.Pain Severity			.85**	4.05	2.26
4.Pain Interference				4.27	2.86

Note. PTSD measured by PCLC; Pain Severity and Interference measured by BPI
** $p < .01$.

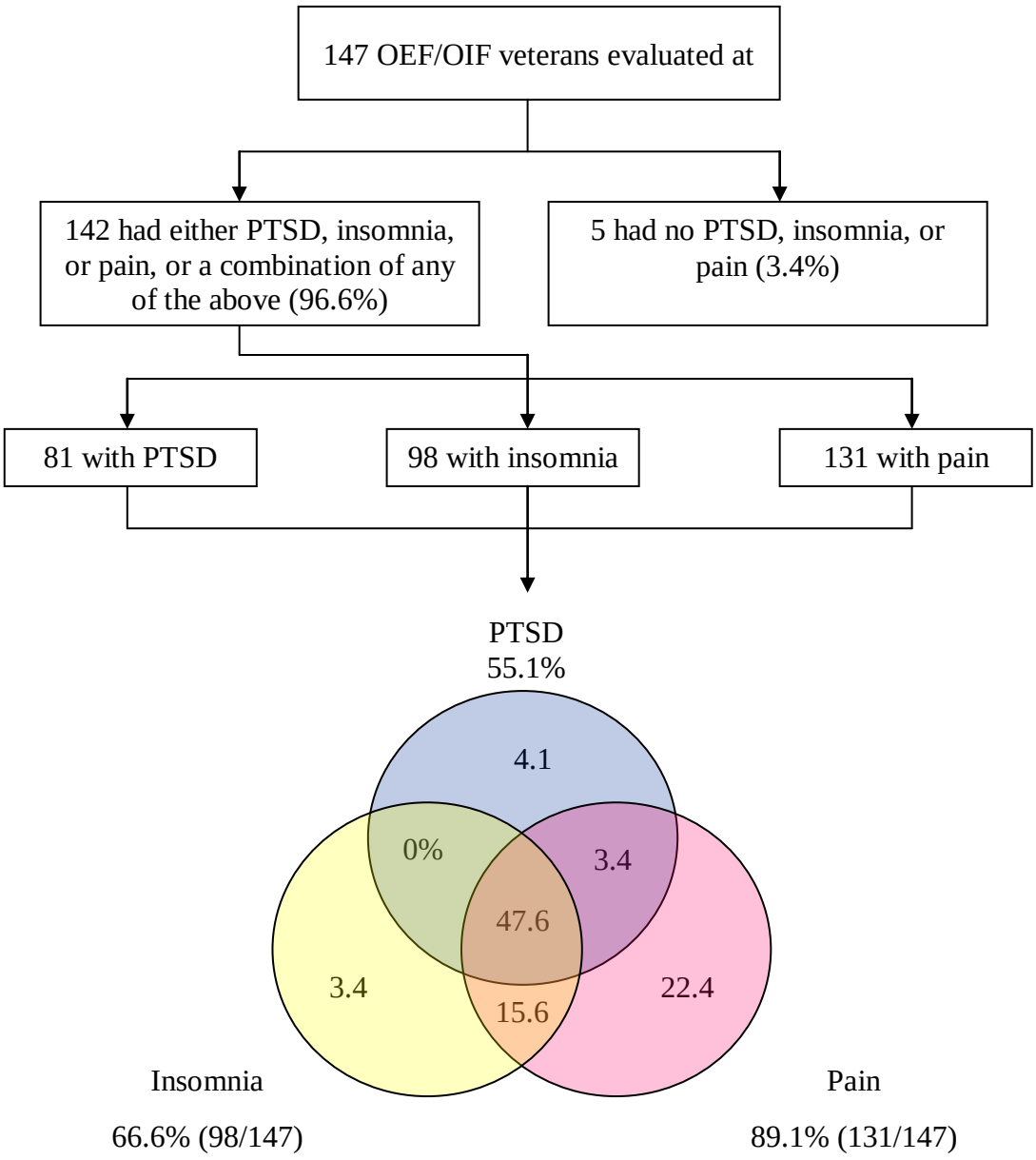

Figure 1. Distribution of veterans with posttraumatic stress disorder, (PTSD), insomnia, and pain in a sample of 147 Operation Enduring Freedom/ Operation Iraqi Freedom (OEF/OIF) veterans evaluated at Memphis Veterans Affairs Medical Center (VAMC).

Insomnia as a Mediator between PTSD and Pain Severity

Analyses were conducted to determine whether insomnia mediated the relationship between PTSD and pain severity in the veteran sample. In the first step of the multiple regression model PTSD significantly predicted insomnia (*a*-path), in the second step insomnia significantly predicted pain severity (*b*-path), and in the third step PTSD significantly predicted pain severity (*c*-path). In the last step pain severity was regressed on both PTSD and insomnia (*c'*-path) to determine whether the mediator accounted for the variance associated with pain severity. The results of this model provided support for insomnia as a partial mediator (see Figure 2). This was confirmed with the bootstrapping technique (Preacher & Hayes, 2008), as zero fell outside the 95% confidence interval [LL = .021, UL = .058] around the indirect effect (*c'*-path). The mediation model accounted for 35% of the variance in pain severity, $R^2 = .35$, $F(2, 144) = 41.14$, $p < .01$ (see Table 2), and suggests that insomnia severity may partially account for the relation between PTSD symptoms and pain severity.

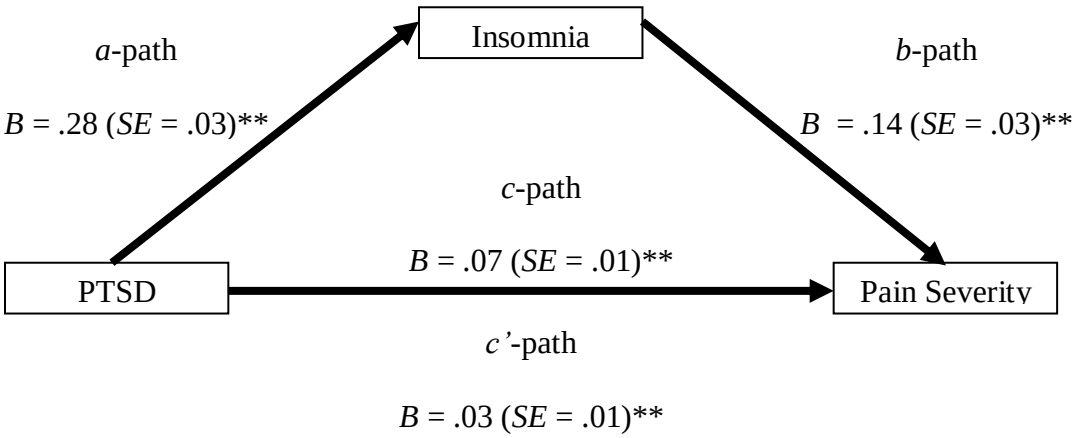

Figure 2. Mediation Model of the Direct and Indirect Effect of PTSD on Pain Severity. ** $p < .01$.

Table 2
Regression and Bootstrap Analyses of the Mediating Role of Insomnia between PTSD and Pain Severity

Criterion Predictor	*B (SE)*	*β*	R^2	LL^a	UL^a
Step 1 (*a*-path)					
Insomnia					
PTSD	.28 (.03)**	.64	.41		
Step 2 (*b*-path)					
Pain Severity					
Insomnia	.14 (.03)**	.58	.33		
Step 3 (*c*-path)					
Pain Severity					
PTSD	.07 (.01)**	.51	.26		
Step 4 (*c'*-path)					
Pain Severity					
PTSD	.03 (.01)**	.23	.36	.02	.06
Insomnia	.04 (.01)**	.43			

[a] Bootstrap test results presented as BCa 95% confidence intervals (CI). CIs containing zero are not significant. LL = lower limit; UL = upper limit; BCa 95% CI = bias corrected and accelerated bootstrapping confidence intervals that include corrections for both median bias and skew (MacKinnon, Lockwood, & Williams, 2004).
** $p < .01$.

Insomnia as a Mediator between PTSD and Pain Interference

Analyses were conducted to determine whether insomnia mediated the relationship between PTSD and pain interference in the veteran sample. In the first step of the multiple regression model PTSD significantly predicted insomnia (*a*-path), in the second step insomnia significantly predicted pain interference (*b*-path), and in the third step PTSD significantly predicted pain interference (*c*-path). In the last step pain interference was regressed on both PTSD and insomnia (*c'*-path) to determine whether the mediator accounted for the variance associated with pain interference. The results of this model provided support for insomnia as a partial mediator (see Figure 3). This was confirmed with the bootstrapping technique (Preacher & Hayes, 2008), as zero fell outside the 95% confidence interval [LL = .026, UL = .069] around the indirect effect (*c'*-path). The mediation model accounted for 40% of the variance in pain interference, R^2 = .40, F(2, 144) = 48.78, $p < .01$ (see Table 3), and suggests that insomnia severity may partially account for the relation between PTSD symptoms and pain interference.

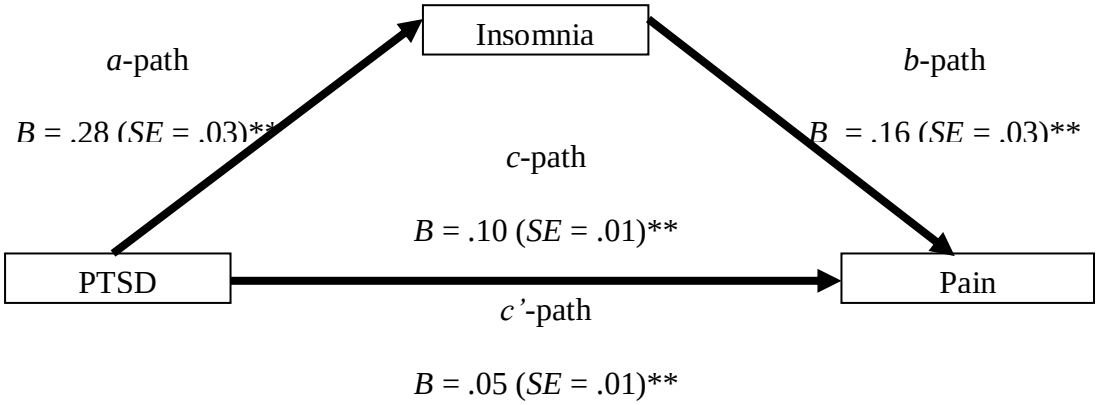

Figure 3. Mediation Model of the Direct and Indirect Effect of PTSD on Pain Interference.
** $p < .01$.

Table 3
Regression and Bootstrap Analyses of the Mediating Role of Insomnia between PTSD and Pain Severity

Criterion Predictor	*B (SE)*	*β*	R^2	LL^a	UL^a
Step 1 (*a*-path)					
Insomnia					
PTSD	.28 (.03)**	.64	.41		
Step 2 (*b*-path)					
Pain Interference					
Insomnia	.16 (.03)**	.59	.35		
Step 3 (*c*-path)					
Pain Interference					
PTSD	.10 (.01)**	.56	.31		
Step 4 (*c'*-path)					
Pain Interference					
PTSD	.05 (.01)**	.30	.40	.03	.07
Insomnia	.05 (.01)**	.40			

[a] Bootstrap test results presented as BCa 95% confidence intervals (CI). CIs containing zero are not significant. LL = lower limit; UL = upper limit; BCa 95% CI = bias corrected and accelerated bootstrapping confidence intervals that include corrections for both median bias and skew (MacKinnon, Lockwood, & Williams, 2004).
** $p < .01$.

CHAPTER 4

DISCUSSION

The purpose of this study was to explore what role sleep disorders, particularly insomnia, played in the relation between PTSD and pain-related outcomes in a sample of OEF/OIF veterans exposed to TBI. These three conditions co-occurred in 47.6% of the veterans, indicating a moderately high prevalence that is similar to rates reported in previous studies of veterans (Hoge et al., 2004 & 2008; Lew et al., 2010; Sayer et al., 2008; Seal et al., 2007; Zeitzer et al., 2009). We also found support for our hypothesis that veterans who reported symptoms consistent with a diagnosis of PTSD reported significantly more insomnia and pain symptoms. These results clearly demonstrate the extent to which PTSD, insomnia, and pain symptoms overlap among veterans exposed to TBI; reinforcing the importance of the polytrauma clinical triad (Lew et al., 2009) and highlighting the role of sleep disturbances in complicating diagnosis and treatment of veterans.

Our primary hypothesis that insomnia functions as a partial mediator in the relation between PTSD and pain-related outcomes was also supported, suggesting that insomnia severity may partially account for the relation between PTSD and pain severity and interference. From the literature, one suggested mechanism for the comorbidity between PTSD and pain is the overlap of cognitive, affective, and behavioral symptoms where PTSD maintains and exacerbates components of chronic pain and vice versa (Defrin et al., 2008). Our findings corroborate this hypothesis by suggesting that sleep disturbances are a mediating link between PTSD and pain.

Sleep disturbances are a core feature of PTSD and are particularly prevalent among combat veterans (APA, 2000; Inman et al., 1990; Mellman et al., 1995; Neylan et al., 1998), with commonly reported sleep complaints being consistent with a subjective report of insomnia (Lavie et al., 1979; Mikulincer, Glaubman, Wasserman, & Porat, 1989). Results of the present mediation model suggest that there are intermediate mechanisms linking sleep complaints with both PTSD and pain. This may be due to the hyperarousal symptom cluster of PTSD reducing overall sleep quality (Germain et al., 2008) and amount of time spent in slow wave sleep (Kobayshi et al., 2007; Yetkin et al., 2010), both of which are associated with reduced pain thresholds (Hakkoinen et al., 2001).

Limitations

Certain limitations warrant mention. The data for this study are cross sectional in nature, which limits the inferences that can be made from the casual meditation model. Although we found support for insomnia as a mediating variable, it is possible that increased pain also contributes to the sleep disturbances noted. Additionally, the finding of insomnia operating as a partial mediator in our sample indicates that this measure of sleep disturbances is only explaining a proportion of the variance in the relation between PTSD and pain severity and interference. It is likely the case that PTSD directly impacts pain in various ways and that other important situational, environmental, or personality variables contribute to this association as well.

This veteran sample was categorized as having been exposed to a TBI during military combat. This assumption was based on veterans' first level screen during their mandatory post-deployment health evaluation conducted at the VA. The sensitivity and

specificity of this 4-item screening measure has come under question and recent research suggests that using all four items as a cutoff the measure has a 40% false negative rate (Terrio, Nelson, Betthauser, Harwood, & Brenner, 2011). Recommendations include using only the first two items as a screen and then conducting additional assessment procedures, such as a structured clinical interview, to evaluate presence of TBI (Terrio et al., 2011). There may also be a financial benefit in veterans receiving diagnoses from the VA and that may have influenced the prevalence rates among the sample. However, this issue is common to all VA settings and therefore does not limit the extent to which our results can be generalized to other veteran samples.

Additionally, we did not account for the cause of the brain injury and there is evidence that rates of PTSD and other associated disorders may differ based on blast or non-blast method of injury (Kennedy et al., 2010; Warden, 2006). The demographics of the present veteran sample are more reflective of the southern geographical region than of all OEF/OIF veterans; with both the unemployment rate (52%) and percentage of African Americans (21%) being higher than national samples (4-8%, 12%, respectively) (Clark, 2012; Helmer, 2011) and therefore, limits the generalizability of the findings. Further, it is possible that this rate of unemployment may be contributing to the prevalence of insomnia symptoms reported in the sample.

Another potential limitation is the high correlation between the pain subscales as measured by the BPI. This was surprising given the theoretical and empirical justification for the existence of multiple dimensions of pain. As stated previously, pain is a subjective experience that can be influenced by a variety of factors including past pain experience, culture, expectations, and context (Bourtwnnais, Perreault, & Bouvette, 2004).

Established dimensions of pain include a sensory and a reactive or interference component (Andrasik et al., 1981; Beecher, 1959; Clark & Yang, 1983; Cleeland & Ryan, 1994). These dimensions as measured by the BPI have been confirmed with factor analysis in veteran populations with both chronic intractable pain and PTSD, where they demonstrated strong convergent and divergent validity (Poundja, Fikretoglu, Guay, & Brunet, 2007; Tan, Jensen, Thornby, & Shanti, 2004). Explanations for the strong correlation in the present study may be that veterans were not attending to the BPI questions, they may have generalized their pain severity to all of the interference areas, or they may have experienced motivating reasons for reporting high pain severity and interference.

Finally, while the BPI is considered one of the gold standards in pain research, insomnia is, by definition a subjective complaint and therefore, may be more challenging to assess. Future studies should consider using sleep studies such as polysomnography to accurately differentiate between common sleep disturbances (i.e., insomnia, sleep apnea, nightmare disorder). Additionally, to increase accuracy in assessing for PTSD symptomatology among military populations, it is has been suggested that the PCL-C measure be followed by a second-tier diagnostic test such as a standardized interview (McDonald & Calhoun, 2012).

Implications

In light of these limitations and the finding of insomnia as only a partial mediator, our results are clinically significant because they highlight the overlap and complexity of presenting complaints in OEF/OIF veterans and the important role of sleep disturbances. This suggests the importance of a multidisciplinary team approach to assessing and

treating these veterans (Lew et al., 2009). This approach should include a focus on sleep disorders as recent research suggests that solely treating PTSD symptoms does not substantially impact areas of sleep, as once thought. Specifically, Belleville and colleagues (2011) evaluated sleep disorders before and after individual cognitive behavioral therapy (CBT) for PTSD and concluded that CBT is helpful in reducing some of the sleep disturbances associated with PTSD but those gains were not maintained after 6 months. Further, a significant proportion (70%) of individuals who began treatment with sleep disturbances still reported problems with sleep at post-treatment. Although this effect has yet to be explicitly examined in OEF/OIF veterans, it provides compelling evidence for the importance of incorporating sleep-specific interventions at the onset of treatment.

Future Directions

Extensions of these findings include looking at which treatment for insomnia would be most helpful in reducing pain outcomes among veterans with PTSD. Various studies have been conducted to examine the efficacy of imagery rehearsal therapy (Moore & Krakow, 2010; Nappi, Drummond, Thorp, & McQuaid, 2009) and CBT for insomnia (CBT-I) both alone (Gellis & Gehrman, 2011) and in combination with exposure, rescripting, and relaxation (Swanson, Favorite, Horin, & Arnedt, 2009). However, there is a lack of consensus on which treatment is best for veterans with PTSD and a lack of treatment studies targeting both PTSD and pain. Further controlled trials are needed to evaluate which treatment approach is most effective in this population and if there are any characteristics of veterans that would assist in treatment modality decisions.

To better understand what parts of sleep are disrupted among veterans with co-occurring PTSD and pain it may be helpful to incorporate a multidisciplinary approach including neurologists and sleep medicine evaluations to understand the ways in which PTSD is contributing to increased insomnia. Additionally, the method of injury (blast vs. non-blast) should be taken into account. Those veterans whose TBI was incurred via blast may be more strongly influenced by the role of insomnia because it has been suggested that they are more affected by the re-experiencing PTSD symptoms (particularly nightmares and flashbacks) (Kennedy et al., 2010). Another important factor to consider in translating this research to effective practice is the low utilization rates among veterans. In one study roughly one half of veterans who screened positive for PTSD actually reported seeking mental health care services (Erbes et al., 2007). The reason for low utilization rates is unclear and investigators should further explore potential barriers to seeking and receiving appropriate treatment. Perhaps a greater focus on insomnia would aid our understanding. Additionally, flagging the co-occurrence of PTSD, insomnia, and pain during screening procedures at the VA and increasing the emphasis of concurrent treatment may help make health care more appealing to a wider range of veterans.

Conclusions

The present findings highlight the importance of evaluating and addressing sleep disturbances in veterans with TBI who are suffering from PTSD and pain. Fortunately, several nonpharmacological treatments for managing sleep have demonstrated efficacy in treating insomnia including stimulus control, sleep restriction, progressive muscle relaxation, cognitive therapy, and biofeedback (Ebben & Spielman, 2009; Perlis, Kuhn,

& Aloia, 2010). Further controlled trials are necessary to evaluate the effectiveness of addressing sleep simultaneously with these common co-occurring conditions among veterans.

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APPENDIX A

PTSD Check List- Civilian Version

Name: _____ Last 4: _____ Date: _____

PCL-C

Below is a list of problems and complaints that veterans sometimes have in response to stressful life experiences. Please read each one carefully, put an "X" in the box to indicate how much you have been bothered by that problem *in the last month*.

	Response:	Not at all (1)	A little bit (2)	Moderately (3)	Quite a bit (4)	Extremely (5)
1.	Repeated, disturbing *memories, thoughts,* or *images* of a stressful experience from the past?					
2.	Repeated, disturbing *dreams* of a stressful experience from the past?					
3.	Suddenly *acting* or *feeling* as if a stressful experience *were happening again* (as if you were reliving it)?					
4.	Feeling *very upset* when *something reminded* you of a stressful experience from the past?					
5.	Having *physical reactions* (e.g., heart pounding, trouble breathing, or sweating) when *something reminded* you of a stressful experience from the past?					
6.	Avoid *thinking about* or *talking about* a stressful experience from the past or avoid *having feelings* related to it?					
7.	Avoid *activities* or *situations* because *they remind you* of a stressful experience from the past?					
8.	Trouble *remembering important parts* of a stressful experience from the past?					
9.	Loss of *interest in things that you used to enjoy?*					
10.	Feeling *distant* or *cut off* from other people?					
11.	Feeling *emotionally numb* or being unable to have loving feelings for those close to you?					
12.	Feeling as if your *future* will somehow be *cut short*?					
13.	Trouble *falling* or *staying asleep*?					
14.	Feeling *irritable* or having *angry outbursts*?					
15.	Having *difficulty concentrating*?					
16.	Being *"super alert"* or watchful on guard?					
17.	Feeling *jumpy* or easily startled?					
18.	Is any of your distress due to loss of someone close to you?					

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APPENDIX B

Insomnia Severity Index

ISI

For each question, please CIRCLE the number that best describes your answer regarding your insomnia within the past TWO WEEKS.

Insomnia problem	None	Mild	Moderate	Severe	Very severe
1. Difficulty falling asleep	0	1	2	3	4
2. Difficulty staying asleep	0	1	2	3	4
3. Problem waking up too early	0	1	2	3	4

4. How SATISFIED/DISSATISFIED are you with your CURRENT sleep pattern?

Very Satisfied	Satisfied	Moderately Satisfied	Dissatisfied	Very Dissatisfied
0	1	2	3	4

5. How NOTICEABLE to others do you think your sleep problem is in terms of impairing the quality of your life?

Not at all Noticeable	A Little	Somewhat	Much	Very Much Noticeable
0	1	2	3	4

6. How WORRIED/DISTRESSED are you about your current sleep problem?

Not at all Worried	A Little	Somewhat	Much	Very Much Worried
0	1	2	3	4

7. To what extent do you consider your sleep problem to INTERFERE with your daily functioning (e.g. daytime fatigue, mood, ability to function at work/daily chores, concentration, memory, mood, etc.) CURRENTLY?

Not at all Interfering	A Little	Somewhat	Much	Very Much Interfering
0	1	2	3	4

Division, 1991. *This is a Government document in the public domain.*

APPENDIX C

Brief Pain Inventory

STUDY ID# _____ HOSPITAL # _____

DO NOT WRITE ABOVE THIS LINE

Brief Pain Inventory (Short Form)

Date: ____/____/____ **Time:** ____

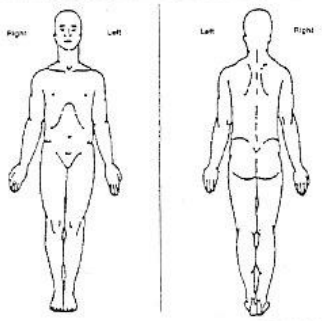
Name: _____ _____ _____

Last First Middle Initial

1. Throughout our lives, most of us have had pain from time to time (such as minor headaches, sprains, and toothaches). Have you had pain other than these every-day kinds of pain today?

1. Yes 2. No

2. On the diagram, shade in the areas where you feel pain. Put an X on the area that hurts the most.



3. Please rate your pain by circling the one number that best describes your pain at its worst in the last 24 hours.

0 No Pain 1 2 3 4 5 6 7 8 9 10 Pain as bad as you can imagine

4. Please rate your pain by circling the one nuimber that best describes your pain at its least in the last 24 hours.

0 No Pain 1 2 3 4 5 6 7 8 9 10 Pain as bad as you can imagine

5. Please rate your pain by circling the one number that best describes your pain on the average.

0 No Pain 1 2 3 4 5 6 7 8 9 10 Pain as bad as you can imagine

6. Please rate your pain by circling the one number that tells how much pain you have right now.

0 No Pain 1 2 3 4 5 6 7 8 9 10 Pain as bad as you can imagine

APPENDIX C (continued)

Brief Pain Inventory

7. What treatments or medications are you receiving for your pain?

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8. In the last 24 hours, how much relief have pain treatments or medications provided? Please circle the one percentage that most shows how much relief you have received.

0%	10%	20%	30%	40%	50%	60%	70%	80%	90%	100%
No Relief										Complete Relief

9. Circle the one number that describes how, during the past 24 hours, pain has interfered with your:

A. General Activity

0	1	2	3	4	5	6	7	8	9	10
Does not Interfere										Completely Interferes

B. Mood

0	1	2	3	4	5	6	7	8	9	10
Does not Interfere										Completely Interferes

C. Walking Ability

0	1	2	3	4	5	6	7	8	9	10
Does not Interfere										Completely Interferes

D. Normal Work (includes both work outside the home and housework)

0	1	2	3	4	5	6	7	8	9	10
Does not Interfere										Completely Interferes

E. Relations with other people

0	1	2	3	4	5	6	7	8	9	10
Does not Interfere										Completely Interferes

F. Sleep

0	1	2	3	4	5	6	7	8	9	10
Does not Interfere										Completely Interferes

G. Enjoyment of life

0	1	2	3	4	5	6	7	8	9	10
Does not Interfere										Completely Interferes