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Impact of PTSD on post-concussive symptoms, neuropsychological functioning, and pain in post-9/11 veterans with mild traumatic brain injury

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ABSTRACT

Prior work suggested that post-traumatic stress disorder (PTSD) worsens post-concussive symptoms (PCS), neuropsychological functioning, and pain-related outcomes in post-9/11 veterans. However, the impact of PTSD in the context of mild traumatic brain injury (mTBI) is not entirely clear. We evaluated possible differences among veterans with deployment-related mTBI with and without PTSD, and a comparison group. We hypothesized that veterans with comorbid mTBI and PTSD would report more PCS, perform worse on neuropsychological tasks, and report greater pain intensity and maladaptive pain coping relative to those without PTSD. Ninety (15 female, 75 male) post-9/11 veterans completed measures of psychiatric functioning, PCS, deployment-related mTBI, pain intensity, pain coping, and a brief neuropsychological evaluation. Veterans with comorbid mTBI and PTSD reported significantly higher PCS across domains, and greater pain intensity and maladaptive coping. They also performed more poorly on measures of recall, but not on measures of attention, encoding, or executive functioning. Findings suggest that PTSD results in greater PCS in the context of mTBI, and is associated with greater pain catastrophizing, worse recall, greater pain intensity, and greater illness-focused coping than in mTBI alone. PCS symptoms, recall, and pain coping may be of clinical importance for post-9/11 veterans with the "polytrauma triad."

1. Introduction

U.S. military veterans of Operations Enduring Freedom and Iraqi Freedom (OEF/OIF) have an elevated risk of developing post-traumatic stress disorder (PTSD) compared to the general population, with a recent meta-analysis suggesting a 23% overall prevalence rate (Fulton et al., 2015). Moreover, one of the most common injuries sustained by approximately 2 million OEF/OIF/Operation New Dawn (OND) veterans is combat-related traumatic brain injury (TBI), with prevalence estimates of mild TBI (mTBI) ranging from 12–23% (O' Neil et al., 2013; Terrio et al., 2009) of these veterans experiencing these injuries secondary to blasts, objects hitting head, falls, motor vehicle accidents, and other combat-related situations (Lindquist et al., 2017). A recent study found that 18% of OEF veterans had sustained a mTBI, and that these veterans were more likely to develop PTSD, major depressive disorder, and/or generalized anxiety disorder post-deployment relative to other OEF veterans who had not sustained a mTBI (Stein et al., 2015). Indeed, most OEF/OIF veterans with deployment-related mTBIs receive a comorbid psychiatric diagnosis, which is most commonly PTSD (e.g., Carlson et al., 2010). However, while both mTBI and PTSD have received significant attention in the extant literature, factors differentiating those with mTBI with and without PTSD have not been fully elucidated.

As noted above, psychiatric comorbidity is very common among OEF/OIF veterans who sustain deployment-related TBI. Lindquist et al., (2017) reported higher prevalence of PTSD (62%) in OEF/OIF veterans who had sustained multiple TBIs during deployment relative to those who had sustained a single TBI during deployment (28%) using the National Post-Deployment Adjustment Survey. In a regional study, Carlson et al. (2010) reported that 85% of veterans with a clinically-confirmed TBI met criteria for at least one other psychiatric diagnosis. The odds of being diagnosed with PTSD were three times greater among OEF/OIF veterans with positive TBI screens (61%) relative to those who screened negatively for TBI (18%). Rates of major depressive disorder

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and substance use disorder were twice as high (Carlson et al., 2010). A total of 19% met criteria for and alcohol or substance use disorder. Another recent regional study of OEF/OIF/OND veterans yielded similar results, with over 80% of subjects who had sustained a TBI meeting criteria for PTSD, and over 35% meeting criteria for a depressive disorder (McGlinchey et al., 2017). In sum, comorbid PTSD and other psychiatric diagnoses are clearly a major clinical consideration for OEF/OIF veterans with TBI (including mTBI).

Relatedly, concerns regarding persistent post-concussive symptoms (PCS) are quite common among OEF/OIF veterans who have sustained a mTBI (Baldassarre et al., 2015). Although some prior research on PCS has suggested that there are independent effects of mTBI regardless of PTSD on PCS (Baldassarre et al., 2015; Brenner et al., 2010), other work has suggested that when accounting for PTSD, mTBI has either a reduced (Wilk et al., 2012) or no effect on PCS (Belanger et al., 2009; Verfaellie et al., 2013). Cognitive PCS are particularly prominent – in a national study, 72% of veterans reported moderate to severe cognitive dysfunction on a self-report inventory who had screened positive for deployment-related mTBI (regardless of whether the mTBI was clinically confirmed). Relative to OEF/OIF veterans with no mTBI, the highest risk for self-reported cognitive dysfunction occurred in the context of comorbid PTSD and major depressive disorder, while mTBI alone accounted for only a small increased risk (Seal et al., 2016). Similar findings were reported in a separate sample of OEF/OIF veterans by Cooper et al. (2011), who noted that higher PTSD symptoms were associated with greater self-reported cognitive dysfunction. Additional studies are needed to further elucidate the impact of mTBI on PCS relative to PTSD symptoms, as the interaction of these conditions likely impacts day-to-day clinical presentations.

These findings from studies assessing cognitive PCS are generally consistent with objective neuropsychological studies of OEF/OIF veterans. When comparing OEF/OIF veterans with PTSD to those with PTSD and mTBI, Soble et al. (2013) found no neuropsychological functioning differences between groups, suggesting that PTSD symptoms are likely associated with cognitive complaints. Similarly, Nelson et al. (2012) found OEF/OIF veterans with only Axis I psychiatric disorders, and veterans with comorbid Axis I/mTBI had large effects ($d = 0.98$ and $d = 0.95$, respectively) on neuropsychological functioning relative to veteran controls. However, veterans with only mTBI did not differ on neuropsychological functioning relative to veteran controls, suggesting that neuropsychological deficits are likely driven by psychiatric symptoms (Nelson et al., 2012). Shandera-Ochsner et al. (2013) reported similar findings, noting that OEF/OIF/OND veterans with PTSD were more likely to demonstrate neuropsychological deficits, regardless of mTBI status. When assessing mTBI severity among OEF/OIF veterans, Verfaellie et al. (2014) found no differences in neuropsychological functioning when comparing three groups exposed to blasts during deployment (no TBI, mTBI with no loss of consciousness, and mTBI with loss of consciousness). However, they reported that symptoms of PTSD and depression were consistently associated with neuropsychological performance. In contrast, Gordon et al. (2011) found no differences in neuropsychological functioning when comparing a smaller sample of OEF/OIF veterans with mTBI with and without other psychiatric conditions. Moreover, Combs et al. (2015) noted possible independent, mild effects of mTBI on processing speed and visual attention in OEF/OIF veterans, although the most significant effects on neuropsychological functioning in their sample were attributed to comorbidity of mTBI with PTSD. Taken together, these studies of neuropsychological functioning among OEF/OIF veterans suggest that objective cognitive deficits are most often associated with PTSD or other psychiatric symptoms as opposed to mTBI, although there is a small degree of variability across studies of this population. Additional studies exploring the impact of mTBI and PTSD on cognition would help to clarify prior findings in post-9/11 veterans, and also inform clinicians with regard to making treatment recommendations for their patients.

In addition to PCS and neuropsychological functioning deficits, pain symptoms are also highly comorbid within this population, with as many as 42% reporting clinically significant symptoms within all three domains (i.e., the “polytrauma triad” of mTBI, PTSD, pain; Otis et al., 2011; Tan et al., 2009). Some of the prior literature has focused on comparing patients with chronic pain to those with chronic pain and PTSD. Consistently, those with higher PTSD symptoms report greater pain intensity (Outcalt et al., 2014; Runnals et al., 2013), greater pain catastrophizing (Morasco et al., 2013; Alschuler and Otis, 2012), and other maladaptive coping strategies such as illness-focused coping (Morasco et al., 2013). However, the literature is more limited with respect to the comorbidity of mTBI, PTSD, and pain in this population. Stojanovic et al., (2016) noted that veterans who had comorbid mTBI + PTSD demonstrated much higher self-reported pain intensity relative to subjects with only one of the conditions or a control group, indicating that there was no effect of mTBI alone on pain intensity. In contrast, other work has suggested that mTBI may have unique effects on pain (e.g., Romesser et al., 2012). Despite high rates of comorbidity of these conditions in OEF/OIF veterans (Otis et al., 2011), there is limited research on how each condition might impact the others in isolation. It also remains unclear if there are differences between OEF/OIF/OND veterans with mTBI with and without PTSD with regard to pain coping strategies. Such differences would be of high clinical relevance, as specifying pain coping strategies to address during treatment would give providers additional treatment planning considerations.

Taken together, these studies demonstrate that while PTSD may have an effect on PCS, neuropsychological functioning, and pain symptoms in OEF/OIF/OND veterans, the potential independent effects of comorbid mTBI on PCS and pain coping strategies have not been fully elucidated. Given the high prevalence of polytrauma in the OEF/OIF/OND veteran population, disentangling these effects have high clinical relevance. For the purpose of our study, we will use “post-9/11 veterans” to describe our sample, which is inclusive of OEF, OIF, and OND veterans. In the present study, we examined whether PCS, cognitive variables, and multiple pain-related measures differentiated post-9/11 veterans with deployment-related mTBI that did not develop PTSD (mTBI-PTSD) from those with deployment-related mTBI that were later diagnosed with PTSD (mTBI + PTSD). We also included a comparison group without either condition (No mTBI/PTSD) as a frame of reference. Based on prior studies discussed above, we hypothesized that post-9/11 veterans with mTBI + PTSD would self-report more PCS across all subdomains compared to both other groups, and that the mTBI-PTSD group would self-report more cognitive dysfunction than the No mTBI/PTSD group. We also predicted that the mTBI + PTSD group would perform worse than the other two groups across all objective neuropsychological domains. We also hypothesized that those in the mTBI + PTSD group would report significantly more pain intensity, pain catastrophizing, and illness-focused coping relative to both other groups. Given the limited prior literature, we made no prediction regarding the mTBI-PTSD relative to the No mTBI/PTSD group on pain measures.

2. Method

This study was approved by the Institutional Review Boards at Jesse Brown VA Medical Center as well as the University of Illinois-Chicago. Research was conducted in accordance with the Helsinki Declaration.

2.1. Participants and procedure

One-hundred twenty-eight participants were selected from a larger sample of post-9/11 U.S. military veterans who were recruited from Jesse Brown VA Medical Center in Chicago, IL between 2012 and 2017. The larger study evaluated biomarkers of PTSD symptoms in post-9/11 veterans, with only minimal exclusion criteria described below.