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Longitudinal Interactions Of Pain Symptoms And Posttraumatic Stress Disorder In U.S. Military Service Members Following Blast Exposure

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Abstract

Military personnel returning from conflicts in Iraq and Afghanistan often endorse pain and posttraumatic stress disorder (PTSD) symptoms, either separately or concurrently. Associations between pain and PTSD may be further complicated by blast exposure from explosive munitions. Although many studies have reported on the prevalence and disability associated with polytraumatic injuries following combat, less is known about symptom maintenance over time. Accordingly, this study examined longitudinal interactive models of co-occurring pain and PTSD symptoms in a sample of 209 military personnel ($M_{\text{age}} = 27.4$ years, $SD = 7.6$) who experienced combat-related blast exposure. Autoregressive cross-lagged analysis examined longitudinal associations between self-reported pain and PTSD symptoms over a one-year period. The best-fitting model indicated that pain and PTSD were significantly associated with one another across all assessment periods, $\chi^2(3) = 3.66$, $p = .30$; TLI = .98; CFI = 1.00; RMSEA = .03, and PTSD had a particularly strong influence on subsequent pain symptoms. The relationship between pain and PTSD is related to older age, race, and traumatic brain injury characteristics. Results further the understanding of complex injuries among military personnel and highlight the need for

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comprehensive assessment and rehabilitation efforts addressing the interdependence of pain and co-occurring mental health conditions.

Perspective—This longitudinal study demonstrates that pain and posttraumatic stress disorder strongly influence one another and interact across time. These findings have the potential to inform the integrative assessment and treatment of military personnel with polytrauma injuries and who are at risk for persistent deployment-related disorders.

Keywords

Chronic Pain; Stress Disorders; Post-Traumatic; Military Personnel; Blast Injuries; Longitudinal Studies

Significant numbers of military personnel returning from Operations Enduring Freedom, Iraqi Freedom, and New Dawn (OEF/OIF/OND) endorse pain and posttraumatic stress disorder (PTSD) symptoms, often concurrently. Estimates show that up to 20% of OEF/OIF/OND Veterans meet criteria for PTSD^{14,32}, and upwards of 81% of OEF/OIF/OND Veterans report ongoing or new pain following their military service^{10,21}. Further, these symptoms frequently co-occur, representing a common polytrauma cluster of injuries. Polytrauma injuries are often associated with exposure to blasts, such as those caused by improvised explosive devices and other explosive munitions³⁵. Blast exposures have resulted in a complex array of outcomes for military personnel, including psychiatric disorders and pain^{9,21}. Research evidence suggests that rates of pain and PTSD among OEF/OIF/OND veterans^{10,14,21,32} are elevated in comparison to civilian samples^{12,13,18,19,30,33}, highlighting the need for comprehensive research and clinical interventions focused on military and veteran populations. Moreover, the comorbidity of pain and PTSD is related to greater affective distress, higher levels of life interference, greater disability, and higher health care utilization than for individuals with either disorder independently^{26,42,44}. The high comorbidity and complexity of these conditions complicates the understanding of their etiology, clinical presentation, and treatment.

Etiologic models of pain and co-occurring mental health disorders purport a complex interaction of biological and psychosocial factors. Prevalence of pain symptoms increases with age^{8,27}, and may also vary among demographic characteristics such as education²⁷, socioeconomic status¹, and gender¹⁷. Complaints of pain are commonly reported in patients who have experienced traumatic life events, suggesting that lifetime exposure to trauma and stress may be an important risk factor for pain disorders^{40,44}. However, other studies have not fully supported these risk and comorbidity models²³, suggesting that correlates of pain and stress-related disorders, including PTSD, may not be fully understood. Several theoretical models propose connections between pain and PTSD^{2,9,16,39}, which consider the interactive contributions of cognitive, emotional, and behavioral responses that mutually reinforce both conditions. For example, PTSD symptoms may reduce pain tolerance, thereby influencing emotional distress, promoting avoidance behaviors, and increasing perceived disability levels^{2,44}. However, less is known regarding the interaction of PTSD and pain in the context of blast injuries; additional blast-related consequences such as traumatic brain injury (TBI) may complicate the understanding of etiology, assessment, and course of treatment in the context of comorbid pain and PTSD³⁵.

Existing work on the co-occurrence of pain and PTSD has primarily relied on cross-sectional prevalence studies, and longitudinal examinations of these conditions are few in number^{12,16,39}. For example, while previous work has supported a longitudinal relationship between pain and PTSD symptoms, results regarding the direction of causality¹² and predictive influence of these symptoms over extended follow-up periods¹⁶ have been mixed. Further longitudinal study is needed to provide a more comprehensive understanding of symptom onset and maintenance, particularly within the context of polytraumatic injury, TBI, and military samples.

The lines of research concerning comorbidity, etiology, and longitudinal associations of pain and PTSD have provided a foundation for further work in this area, and highlight the need for nuanced analysis of the temporal relationship between pain and PTSD symptoms. The present study investigates the longitudinal course of pain and PTSD symptoms in a sample of active duty military service members and veterans following blast exposure. This study addresses several gaps in the literature by examining longitudinal associations between pain and PTSD symptoms within the context of combat-related blast injuries, and utilizing an autoregressive methodology to examine the temporal associations between these variables and relevant covariates (i.e., age, race, injury characteristics). Based on previous research supporting an interactive model of pain and PTSD, we hypothesized that: (1) pain and PTSD symptoms would be significantly associated over time, (2) pain symptoms would predict subsequent PTSD symptoms, (3) PTSD symptoms would predict subsequent pain symptoms, and (4) the relationship between pain and PTSD symptoms would be impacted by the covariates of age, race, and severity of blast exposure.

Materials and Methods

Data were collected as part of an ongoing Congressionally Directed Medical Research Program-funded investigation of post-combat injuries from blast exposure during OEF/OIF/OND. Eligible military service members and veterans had a blast experience within the past two years while deployed in OEF/OIF/OND. The participants were assessed at three time points over a one-year period: baseline (Time 1, or “T1”), after six months (Time 2, or “T2”), and after 12 months (Time 3, or “T3”). The baseline assessment is defined as the time at which the participant entered the study, and the average time between the date of the worst identified blast exposure and the initial assessment period was 519.0 days ($SD = 541.1$).

Procedure

The relevant Institutional Review Boards approved this study, and informed consent was obtained after the details of the study were thoroughly explained to participants. All participants completed a series of questionnaires. Although many were enrolled at clinics, the research evaluations were separate from clinical care or compensation and pension processes. Research staff supervised completion of all the questionnaires and provided additional instructions as needed.

Participants

Participants were military service members and veterans recruited via letters, advertisements, and from ambulatory healthcare clinics at a mid-Atlantic VA Medical Center and at several Army and Marine Corps bases located in the mid-Atlantic region of the United States. For the present analyses, participants who reported at least one blast experience during combat were included in the study ($N = 209$). The sample consisted of 202 men and seven women, who were on average 27.4 years of age ($SD = 7.6$) at the baseline assessment. Many of the respondents reported more than one deployment location (Table 1).

Measures

Short Form McGill Pain Questionnaire (SF-MPQ)²²—Participants were asked to rate current levels of general pain symptoms. This pain rating scale consists of 15 pain descriptors (11 sensory, four affective) that are rated for intensity on a Likert scale from 0 (“none”) to 3 (“severe”). The scale yields three pain scores: a total pain score, which is a sum of all 15 items, and sensory and affective pain subscale scores. The total pain score is frequently used in research and clinical applications, with higher scores indicating greater severity of current pain symptoms. The SF-MPQ has been shown to have strong psychometric properties, and is sensitive to changes in pain scores over time and/or as a result of clinical intervention²². Internal consistency for the total SF-MPQ score in the current sample was good (Cronbach's $\alpha = 0.86$).

Prior Health and Demographics Questionnaire—A detailed health and demographics questionnaire was developed for the study. Questions assessed for basic demographic information (e.g., sex, age, marital status, race/ethnicity, education, military history) as well as selected psychiatric and medical histories, which were not the focus of the present study. Age was included in the analyses as a continuous variable, and race was categorized as White/Caucasian, African-American, or Other Race. The race variables were dummy coded for analysis, with White/Caucasian as the reference group.

Blast Experience Screening Questionnaire (BESQ)—Participants were queried on their traumatic blast experience(s) via the BESQ, which was developed for a larger epidemiologic study of blast exposures. The BESQ was adapted from the Walter Reed Army Medical Center Blast Injury Questionnaire (WRAMC BIQ)³⁶. The WRAMC BIQ screens patients for previously unreported blast-related pathologic conditions via 19 questions regarding the blast itself, as well as pre- and post-blast symptoms including the presence of visual disturbances, headaches, dizziness, or hearing loss, distance from the blast, and degree of cover. The BESQ focuses on symptoms immediately after the blast exposure, and also inquires about alterations of consciousness (AOC) following the blast. The AOC questions were designed to assess three specific aspects of post-blast severity: memory gap, observer-reported loss of consciousness, and continuous memory. Respondents are asked to provide information on up to three separate blast events, which included a request to identify the “worst” blast event. For the purposes of this study, only information regarding the worst blast event was used to calculate the TBI characteristics. In accordance with previous work with this scale⁴⁵, responses from the selected AOC questions indicating post-traumatic

amnesia (PTA) or loss of consciousness (LOC) were combined to create a categorical index of three potential diagnostic groups of mild TBI: definite/probable TBI (two or three positive AOC items); possible TBI (one positive AOC item), and no evidence of TBI with either PTA or LOC (all three AOC items negative; see ⁴⁵ for development of the scoring system). The TBI diagnostic classification variables were dummy coded for analysis, with “no evidence of TBI” as the reference group.

PTSD Checklist (PCL)⁴⁶—The PCL is a 17-item self-report measure of the 17 *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV) symptoms of PTSD. The scale is commonly used to screen individuals for PTSD, aid in diagnostic assessment of PTSD, and monitor change in PTSD symptoms²⁵. Respondents are asked, “In the past month, how much have you been bothered by...” each symptom, rated on a Likert scale from 1 (“not at all”) to 5 (“extremely”). In the current study, the PCL total score was used as a measure of PTSD symptom severity, and the internal consistency in the current sample was excellent (Cronbach's $\alpha = 0.93$).

Statistical Analyses

Missing Data Analysis—Of the $N = 209$ participants assessed at T1, only $n = 125$ completed T2 assessments and $n = 112$ completed T3 assessments. Due to substantial attrition, data were explored for patterns in missingness. In addition to exploring potential differences in baseline TBI classification, PTSD symptoms, and pain symptoms as contributing factors to attrition, several demographic variables and military service variables (i.e., age, race, deployment location, and military service branch) were also investigated. Missing data at each follow-up assessment period (i.e., T2, T3, and missing at both time points) were coded as a binary variable (1 = missing, 0 = not missing). Preliminary comparisons applied the χ^2 statistic and the F statistic (utilizing the SPSS version 20 Compare Means command) for the categorical and continuous variables, as appropriate. These analyses were followed by logistic regression analyses to determine which variables predicted missingness at each follow-up period.

Autoregressive Models—Autoregressive models are also known as Markov simplex or univariate simplex models. These models describe change in a variable over time in terms of the measurement of that variable on previous measurement occasions. A first-order autoregressive model only accounts for the measurement immediately prior to the one of interest. In other words, pain symptoms at time t are predicted only by pain symptoms at time $t-1$, and pain symptoms at any earlier time point have no direct impact on pain at time t . Second-order parameters may be added to the model to estimate additional pathways (i.e., pain at time t is predicted by pain at time $t-2$). A univariate model (i.e., a focus on only one variable) can then be extended to the multivariate case in order to model two or more distinct variables over time. In the present study, pain and PTSD symptoms were first modeled using separate univariate autoregressive models to examine each model's ability to adequately describe the respective symptom scores over time. Pain and PTSD scores at each time point (e.g., T2) were regressed onto pain or PTSD scores from the previous assessment period (e.g., T1) to determine the extent to which pain symptoms at one time point are predicted by the pain symptoms from the previous six months, and the extent to which

PTSD symptoms are predicted by PTSD symptoms from the previous six months. In other words, the univariate autoregressive model examines how well scores at one time period predict scores at a subsequent time period, thereby illustrating both the degree of change and pattern of change in a particular variable over time. Fit statistics, described below, identified the best fitting PTSD and pain models before combining the models into a multivariate autoregressive cross-lagged model.

Autoregressive cross-lagged models—The autoregressive cross-lagged model combines separate univariate models and allows the examination of the relationship between multiple processes. For this study, pain symptoms at time t were regressed onto pain symptoms at $t-1$ and PTSD symptoms at $t-1$, and PTSD symptoms at time t were regressed onto PTSD symptoms at time $t-1$ and pain symptoms at $t-1$. This multivariate approach allowed us to examine a bidirectional transactional model of pain and PTSD symptoms by testing the extent to which PTSD symptoms are predicted by pain symptoms at the previous six-month assessment period above and beyond the PTSD symptoms the previous six months, and the extent to which pain symptoms are predicted by PTSD symptoms above and beyond pain symptoms the previous six months. Fit statistics were used to first identify the best fitting cross-lagged model before the covariates of age, race, and TBI classification were added to the model. Then, in a final model, the covariates were added to the cross-lagged model to investigate the influence of these factors on the longitudinal associations between pain and PTSD symptoms.

All analyses were conducted in MPlus, version 6.11²⁴ using maximum likelihood estimation with standard errors that are robust to departures from normality. Modification indices were examined after each iteration to examine the impact of adding potentially meaningful paths not included in the first-order cross-lagged model and determine the best-fitting models. Only pathways that represented theoretically and/or empirically meaningful relationships were added to the models to reduce the likelihood of non-generalizable results. In addition to χ^2 , fit indices were used to evaluate model fit according to the following criteria: the root mean squared error of approximation (RMSEA) at or below 0.05¹⁵, the Tucker–Lewis index (TLI) of 0.95 or higher¹⁵, and the comparative fit index (CFI) of 0.95 or higher¹⁵. The Bayesian Information Criterion (BIC)³⁷ was also used to compare the relative fit of the models. Models with a lower value of the BIC are considered to be better fitting and more parsimonious.

Results

Missing Data

Preliminary exploration of missingness indicated that participants who had missing data at T3 were significantly younger ($M_{\text{age}} = 25.8$, $SD = 6.5$) than those who were not missing, $M_{\text{age}} = 28.8$, $SD = 8.3$, $F(1, 207) = 8.41$, $p < .01$. There were no differences in age for missingness at T2 or at both time periods. There were several patterns in missingness related to deployment location history as reported at the baseline assessment: at T2, there were significantly fewer individuals with missing data who reported two deployments to OEF, compared to those with zero or one OEF deployment, $\chi^2(2) = 6.58$, $p < .05$. An opposite

effect was found at T3, in which those reporting two deployments to OEF were more likely to be missing at the final assessment, $\chi^2(2) = 14.4$, $p < .001$. Among those deployed to OIF, a history of no deployments was associated with attrition at T3, $\chi^2(4) = 9.69$, $p < .05$. Compared to individuals in other service branches and with other post-deployment statuses, those who reported service in the Marines and who were on active duty status following deployment were more likely to be missing at T3, $\chi^2(1) = 12.59$, $p < .001$, and $\chi^2(1) = 9.46$, $p < .01$, respectively. Those in the Army and in the Reserves following deployment were significantly less likely to have missing data at T3, $\chi^2(1) = 11.07$, $p < .001$, and $\chi^2(1) = 10.6$, $p < .001$, respectively. The variables of baseline pain symptoms, PTSD symptoms, TBI classification, and race did not demonstrate any significant differences in attrition at T2, T3, or at both time points.

The variables with statistically significant patterns of missingness from the preliminary analyses were entered into a logistic regression analysis in which each follow-up period (i.e., T2, T3, both time periods) was the binary dependent variable. At T2, only a history of two deployments to OEF contributed significantly to the prediction model, $B(SE) = -1.19(.53)$, 95% CI = .11 - .85, $Exp(B) = .31$, $\chi^2 = 7.15$, $p < .05$. At T3, only post-deployment status in the Reserves, $B(SE) = -1.22(.58)$, 95% CI = .09 - .93, $Exp(B) = .30$, contributed to the model, $\chi^2 = 27.79$, $p < .01$. None of the variables predicted missingness at both time periods. In sum, the final missing data analysis indicated that those deployed to OEF two times were more likely to have complete data (i.e., less likely to be missing) at T2 than those with zero or one OEF deployment, and those in the Reserves post deployment were more likely to have complete data at T3 than those who were not on Reserve status. Notably, neither pain symptoms nor PTSD symptoms nor TBI classification appeared to be related to attrition, and thus the results of the current study are considered to be an accurate depiction of these symptoms over time.

Descriptive Statistics

Descriptive characteristics of the sample are presented in Table 1. Using the diagnostic classification of TBI based on AOC responses, $n = 45$ were considered to have possible TBI, and $n = 70$ were categorized as probable TBI, with the remaining $n = 94$ reporting no symptoms indicative of TBI following blast exposure. All of the PTSD and pain scores were moderately-to-strongly correlated with each other at the three measurement occasions (Table 2). These measures were positively correlated with baseline age. PTSD and pain symptoms were also analyzed for potential differences by TBI classification. For those individuals reporting no symptoms indicative of TBI following blast exposure, the mean baseline total score on the PCL was 45.7 ($SD = 15.5$) and the mean baseline SF-MPQ total score was 8.8 ($SD = 6.7$). Among those classified as possible TBI, the mean PCL and SF-MPQ total scores were 47.9 ($SD = 15.2$) and 12.4 ($SD = 8.6$), respectively. The mean baseline PCL and SF-MPQ total scores were 50.2 ($SD = 13.6$) and 13.1 ($SD = 8.3$), respectively, for those classified as probable TBI. The differences in scores between groups for both the baseline pain symptoms, $F(2, 206) = 7.2$, $p < .001$, and PTSD symptoms, $F(2, 206) = 1.9$, $p = .05$, were statistically significant. At subsequent time points, however, there were no statistically significant differences in pain or PTSD symptoms by TBI classification.

Autoregressive Models

Preliminary analysis of the pain and PTSD symptom scores indicated relative stability and lack of growth in the variables over time. There was not significant change in self-reported pain symptoms over time; however, examination of average PTSD scores showed a slight decrease in symptoms from T2 to T3. Due to the modest growth in the variables, simplex models (i.e., autoregressive or Markov models) were considered the best choice to fit the separate pain and PTSD measures. In these initial models, pain and PTSD symptoms, respectively, were regressed onto the symptoms reported at the six months immediately preceding. These models resulted in acceptable overall model fit indices (Table 3), indicating that pain symptoms at T1 predicted pain at T2; however, pain at T2 did not predict pain at T3. PTSD symptoms at T1 predicted PTSD symptoms at T2, which then predicted PTSD symptoms at T3. The simplex models were included for further analysis in the autoregressive cross-lagged modeling framework.

Autoregressive cross-lagged models

PTSD and pain-only model—The interaction model of pain and PTSD symptoms was evaluated by combining the best fitting pain simplex model and PTSD simplex model above and adding cross-lagged parameters between pain and PTSD scores. The cross-lagged parameters allowed for an examination of the interaction between variables over time by assessing how well one variable (e.g., pain) predicts the other variable (e.g., PTSD) at the same or subsequent assessment period. For the initial step, we analyzed pain and PTSD symptom scores without the covariates. The influence of PTSD symptoms on pain symptoms was tested by regressing pain scores onto PTSD scores from the previous six months, thereby demonstrating the predictive ability of PTSD symptoms for pain symptoms at the following assessment period. Then, to test for the influence of pain on PTSD symptoms, cross-lagged parameters were included that regressed PTSD scores onto pain scores the previous six months. This resulted in good model fit, $\chi^2(4) = 8.44$, $p = 0.08$; TLI = 0.95; CFI = 0.97; RMSEA = 0.07 (0.00 – 0.14); BIC = 6607.12. Within-time associations between the pain and PTSD variables were also statistically significant across all time points, $\beta_{T1} = 56.40$, $p < 0.001$; $\beta_{T2} = 57.81$, $p < 0.001$; $\beta_{T3} = 25.67$, $p < 0.001$, indicating that PTSD and pain symptoms are correlated with one another at a given time point in addition to holding predictive utility for each other at subsequent time points. Modification indices recommended including additional autoregressive parameters for pain measurement at T1 to T3; this resulted in slightly improved model fit, $\chi^2(3) = 2.80$, $p = 0.42$; TLI = 1.00; CFI = 1.00; RMSEA = 0.00 (0.00 – 0.11); BIC = 6606.96.

The cross-lagged parameters indicated that PTSD scores predicted pain scores at each subsequent time point, $\beta_{PTSD1-Pain2} = 0.10$, $SE = 0.05$, $p < 0.05$; $\beta_{PTSD2-Pain3} = 0.15$, $SE = 0.06$, $p < 0.05$. However, pain at T1 only predicted PTSD at T2, $\beta = 0.36$, $SE = 0.14$, $p < 0.05$. The parameter between pain at T2 and PTSD at T3 was not statistically significant, $\beta = 0.07$, $SE = 0.18$, $p = 0.67$ (Figure 1).

Covariate model—Finally, we included the covariates of baseline age, race, and TBI classification in the cross-lagged model. This model resulted in good fit, $\chi^2(3) = 3.66$, $p = 0.30$; TLI = 0.98; CFI = 1.00; RMSEA = 0.03 (0.00 – 0.13); BIC = 6678.31; however, the

model fit indices decreased somewhat from the previous model. As with the previous model, modification indices recommended the addition of a second-order cross-lagged parameter from pain scores at T1 to pain scores at T3 (Figure 1). The covariates were not statistically significant for all parameters. The covariate model indicated the same associations between the pain and PTSD variables as the initial cross-lagged model, and this final model is illustrated in Figure 1. The results suggest that the inclusion of covariates, while clinically meaningful and potentially theoretically important, did not add significant explanatory power to the overall model.

Discussion

This is the first study to examine the longitudinal interactive effects of pain and PTSD symptoms in a military/veteran sample using an autoregressive cross-lagged design. The autoregressive cross-lagged model is a powerful method for exploring the temporal association of two variables over time. Overall, results are consistent with the literature supporting a strong relationship between pain and PTSD symptoms^{16,21,39,44}. The longitudinal nature of the data allowed us to investigate natural interactions of symptoms over time, and the results yielded important insights into the relationship between pain and PTSD in the context of combat-related blast exposure. A better understanding of pain and PTSD symptom maintenance is particularly important for the assessment and treatment of military personnel who have experienced polytrauma injuries and who are at risk for long-term complications as a result of this complex injury profile.

When first considering pain and PTSD symptoms separately, we found that the reported symptoms were relatively consistent across time. Notably, pain scores at T2 and T3 were independently predicted by pain at T1, suggesting that initial pain and/or injury status may be the most important indicator of future pain symptoms. Similar results have been found in other pain samples, in which disability status, pain-related distress, and comorbid psychiatric or personality factors at time of injury have been shown to predict chronicity of pain symptoms, e.g.^{7,29,41}. Despite PTSD symptoms showing a slight decrease over time, on average, the autoregressive cross-lagged models demonstrated that PTSD scores were best predicted by PTSD scores the previous year, as indicated by the large parameter estimates of the autoregressive portion of the model. Thus, while recovery from PTSD symptoms is one common trajectory following trauma exposure^{4,5}, many participants in our sample continued to be affected by significant PTSD symptoms at the 12-month assessment period, as evidenced by average PCL scores that fell within the range of suggested PTSD diagnostic cut-offs (the suggested cut-off for specialized VA primary care clinics and specialized TBI or pain clinics is 36-44²⁵). It is important to note that our assessment period was limited to one year, and there is evidence that spontaneous PTSD recovery may take several years before symptoms significantly remit^{4,5}. The stability of both the pain and PTSD symptoms may also be related to the amount of time between the initial injury and the study's baseline assessment period (approximately 17 months, on average). Symptoms may have had ample time to stabilize and/or become chronic presentations. A shorter injury-to-assessment period and a longer follow-up period of PTSD and pain symptoms will add clarity to the longer-term trajectory of post-combat difficulties.

Consistent with our expectations, we observed significant associations between pain and PTSD symptoms over the three assessment points. Pain and PTSD showed strong within-time correlations in the cross-lagged model. Further, PTSD scores at T1 significantly predicted pain scores at T2 and T3, above and beyond the previous pain scores. Pain predicted PTSD scores above and beyond the previous PTSD scores at T2, but not at T3. The findings suggest that while pain and PTSD appear to interact and influence one another over time, PTSD appears to exert a particularly strong influence on pain scores. Jenewein and colleagues¹⁶ longitudinal study of PTSD and pain symptoms among accident survivors similarly found a mutual maintenance of pain intensity and PTSD symptoms over a six-month period, but at one year, PTSD symptoms were demonstrated to have a significant impact on pain whereas pain was no longer shown to have a significant impact on PTSD. The interactive model of pain and PTSD is supported by theoretical conceptualizations of the co-occurring disorders^{2,38}, and our findings lend empirical support to these conceptual models. In particular, PTSD symptoms appear to have a significant impact on pain. This finding has important theoretical and clinical implications, as symptoms associated with PTSD may prolong comorbid pain, thereby contributing to the chronicity of both presentations and preventing effective rehabilitation. Common behavioral or psychosocial factors, such as hypervigilance to perceived threats and withdrawal from rewarding daily activities, may be an important link between the two conditions¹². Our results suggest that a focus on PTSD symptoms may be an important first step in complementary treatment interventions, as these psychological and behavioral factors appear to influence future pain symptoms. Interventions for the co-occurring disorders may emphasize treatment of PTSD symptoms and consistent, ongoing monitoring of psychological symptoms in order to effectively reduce the long-term difficulties associated with both presentations. Particularly among military personnel, pain complaints may be more commonly reported or viewed as more socially acceptable than PTSD symptoms or other mental health difficulties, and clinical service providers may miss important potential underlying psychological and behavioral contributions to pain.

Finally, we investigated the influence of selected covariates on the interactional model of pain and PTSD symptoms. Older age at the baseline assessment was associated with both pain and PTSD symptoms at T1 and T3, a finding that is largely consistent with previous work on pain and co-morbid disorders, e.g.,^{8,27,34}. White/Caucasian race was related to pain symptoms at T1 and to PTSD symptoms at T3, which is contrary to prior studies suggesting that minority race/ethnicity individuals may be at increased risk for both disorders^{11,20,28,31}. Notably, our sample was chiefly composed of individuals who self-identified as White/Caucasian, and thus there may not have been sufficient power to detect true differences between the race groups and relationships to the symptom variables. Future work with more diverse and representative samples is needed to clarify these associations. The final model also indicated that more severe TBI diagnostic classification status (i.e., probable and possible TBI) was associated with more severe pain and PTSD symptoms at T1. Although the study did not explicitly query for pain or PTSD symptoms related to blast injury, the demonstrated relationship between TBI classification status and symptoms suggest that the blast event has an important additive (if not directly causative) effect on subsequent physical and psychiatric symptoms. This finding highlights the relevance of the initial injury period

to the early stages of polytrauma complaints, as TBI and blast-related symptoms may function as important indicators for identifying those individuals who go on to develop more chronic symptoms. Although the final covariate autoregressive cross-lagged model showed good fit, the covariate model did not demonstrate significant improvements over the model investigating pain and PTSD symptoms alone. Thus, the demographic and injury characteristics of our sample appeared to have a primary influence on initial assessment of pain and PTSD symptoms in our sample, and the interactive relationship regarding pain and PTSD best explained the longitudinal symptom maintenance in our sample.

There were several limitations to this study that must be noted. First, autoregressive cross-lagged models are only one of several methods for examining relationships between variables over time. We selected this model because it allowed us to examine the extent to which symptoms of one disorder (e.g., pain) are predicted by earlier symptom reports of co-occurring symptoms (e.g., PTSD), above and beyond previous reports of pain symptoms. This method does not model growth across all time periods, nor does it consider individual differences in the trajectories of pain and PTSD over time. Combined autoregressive and latent growth curve models have the benefit of modeling time-specific changes in symptoms while taking into account individual growth trajectories⁶. However, we were unable to examine these models due to the relative stability (and thus, absence of significant latent growth factors) for both symptom measures. Another limitation of the study was the attrition rate from baseline to the final assessment; approximately 46% of the original sample did not complete the 12-month assessment. Although missing data analysis did not determine any significant differences in our sample with regard to baseline pain and PTSD symptoms or TBI classification, and our final sample size was adequately powered for the autoregressive modeling framework, more complete data may yield additional findings and insights into comorbid pain and PTSD symptoms and the influence of relevant covariates. Interestingly, missing data analysis found that those participants who reported two OEF deployments were more likely to be Marines and on active duty status post deployment, whereas those individuals in the Reserves were almost predominantly from the Army. These groups were more likely to have complete data at the T2 and T3 follow-up periods, respectively. Although redeployment status and service transitions throughout the assessment periods were not assessed, it may be possible that individuals in the Reserves were less likely to be re-activated for duty or deployment, and therefore more likely to be available for participation in the final assessment period. Similarly, the timing of the T2 assessment may have coincided with deployment schedules such that those with multiple OEF deployments happened to be more readily available for the second assessment.

Further, this study relied on self-reports of pain, PTSD, and TBI symptoms. While self-report assessments can be helpful for assessing an individual's perceptions of distress and difficulties, a limitation of this assessment method is the potential bias in the respondents' self-report of their past experience and symptoms. Moreover, information regarding pre-deployment medical and psychiatric conditions was limited for our sample, and it is unknown whether the reported symptoms indicated new complaints or exacerbations/continuations of existing difficulties. Thus, while this study was able to identify patterns of symptom co-occurrence and mutual maintenance, factors related to symptom onset are less clear; this is a target for future study. We decided to focus on the comorbidity of pain and

PTSD symptoms for the present analyses, but it is well-known that pain is also highly associated with depression symptoms^{3,43}. Future work will investigate the influence of depression on both pain and PTSD symptoms, as this may represent an additional variable that accounts for maintenance of these co-occurring presentations. Finally, the study sample of relatively young, primarily male military service members and veterans reflects a particular composition of military personnel, and the findings may not generalize to the general population or other military/veteran samples. More work is needed to better understand the risk factors and correlates of pain in diverse samples.

In summary, these findings hold important implications regarding clinical interventions for pain and co-occurring psychiatric and medical symptoms in returning service members and veterans. These data indicate an extensive number of returning OEF/OIF/OND military personnel and veterans with polytraumatic injuries who continue to be affected by these symptoms many months following blast exposure. A strength of the present study is the investigation of longitudinal outcomes and comorbidity patterns using a robust data analysis methodology that is well-equipped to determine the interactive relationships between symptoms. Findings from the present study demonstrate that post-deployment symptoms strongly influence one another and interact across time, and PTSD symptoms appear to exert a strong influence on subsequent pain symptoms. Given that pain and PTSD symptoms co-occur frequently and influence one another, it is important to identify both pain and PTSD symptoms in clinical assessment and treatment planning processes. Early clinical interventions and rehabilitation efforts may consider the treatment of both pain and psychiatric symptoms in hopes of optimizing treatment and decreasing the probability that symptoms will persist and become chronic psychological or physical responses to trauma.

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References

1. Andersson HI, Ejlerstsson GR, Leden I, Rosenberg C. Chronic pain in a geographically defined general population: studies of differences in age, gender, social class, and pain localization. *Clin J Pain*. 1993; 9(3):174–82. [PubMed: 8219517]
2. Asmundson GJG, Coons MJ, Taylor S, Katz J. PTSD and the experience of pain: research and clinical implications of shared vulnerability and mutual maintenance models. *Can J Psychiatry*. 2002; 47:930–7. [PubMed: 12553128]
3. Bair MJ, Robinson RL, Katon W, Kroenke K. Depression and pain comorbidity: a literature review. *Arch Intern Med*. 2003; 163(20):2433–45. [PubMed: 14609780]
4. Bonanno GA, Mancini AD, Horton JL, Powell TM, Leardmann CA, Boyko EJ, Wells TS, Hooper TI, Gackstetter GD, Smith TC. Millennium Cohort Study Team. Trajectories of trauma symptoms and resilience in deployed US military service members: prospective cohort study. *Br J Psychiatry*. 2012; 200(4):317–23. [PubMed: 22361018]
5. Bonanno GA. Loss, trauma, and human resilience. Have we underestimated the human capacity to thrive after extremely aversive events? *Am Psychol*. 2004; 59:20–8. [PubMed: 14736317]

6. Curran, PJ.; Bollen, KA. The best of both worlds: Combining autoregressive and latent curve models. In: Collins, LM.; Aline, G., editors. *New Methods for the Analysis of Change Decade of Behavior*. American Psychological Association; Washington, DC: 2001. p. 107-135.
7. Gatchel RJ, Polatin PB, Kinney RK. Predicting outcome of chronic back pain using clinical predictors of psychopathology: a prospective analysis. *Health Psychol.* 1995; 14(5):415–20. [PubMed: 7498112]
8. Gatchel RJ. Comorbidity of chronic pain and mental health disorders: the biopsychosocial perspective. *Am Psychol.* 2004; 59(8):795–805. [PubMed: 15554853]
9. Gibson C. Review of posttraumatic stress disorder and chronic pain: the path to integrated care. *J Rehabil Res Dev.* 2012; 49(5):753–76. [PubMed: 23015584]
10. Girona RJ, Clark ME, Massengale JP, Walker RL. Pain among veterans of operations enduring freedom and Iraqi freedom. *Pain Med.* 2006; 7(4):339–43. [PubMed: 16898945]
11. Green CR, Anderson KO, Baker TA, Campbell LC, Decker S, Fillingim RB, Kalauokalani DA, Lasch KE, Myers C, Tait RC, Todd KH, Vallerand AH. The unequal burden of pain: confronting racial and ethnic disparities in pain. *Pain Med.* 2003; 4(3):277–94. [PubMed: 12974827]
12. Gureje O, Simon GE, Von Korff M. A cross-national study of the course of persistent pain in primary care. *Pain.* 2001; 92:195–200. [PubMed: 11323140]
13. Hardt J, Jacobsen C, Goldberg J, Nickel R, Buchwald D. Prevalence of chronic pain in a representative sample in the United States. *Pain Med.* 2008; 9(7):803–12. [PubMed: 18346058]
14. Hoge CW, Castro CA, Messer SC, McGurk D, Cotting DI, Koffman RL. Combat duty in Iraq and Afghanistan, mental health problems, and barriers to care. *N Engl J Med.* 2004; 351(1):13–22. [PubMed: 15229303]
15. Hu LT, Bentler PM. Cutoff criteria for fit indices in covariance structure analysis: conventional criteria versus new alternatives. *Struct Equ Modeling.* 1999; 6:1–55.
16. Jenewein J, Wittmann L, Moergeli H, Creutzig J, Schnyder U. Mutual influence of posttraumatic stress disorder symptoms and chronic pain among injured accident survivors: a longitudinal study. *J Trauma Stress.* 2009; 22(6):540–8. [PubMed: 19924822]
17. Keogh E, McCracken LM, Eccleston C. Gender moderates the association between depression and disability in chronic pain patients. *Eur J Pain.* 2006; 10(5):413–22. [PubMed: 16009583]
18. Kessler RC, Chiu WT, Demier O, Merikangas KR, Walters EE. Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry.* 2005; 62(6):617–27. [PubMed: 15939839]
19. Kessler RC, Sonnega A, Bromet E, Hughes M, Nelson CB. Posttraumatic stress disorder in the National Comorbidity Survey. *Arch Gen Psychiatry.* 1995; 52(12):1048–60. [PubMed: 7492257]
20. Koenen KC, Stellman JM, Stellman SD, Sommer JF Jr. Risk factors for course of posttraumatic stress disorder among Vietnam veterans: a 14-year follow-up of American Legionnaires. *J Consult Clin Psychol.* 2003; 71(6):980–6. [PubMed: 14622073]
21. Lew HL, Otis JD, Tun C, Kerns RD, Clark ME, Cifu DX. Prevalence of chronic pain, posttraumatic stress disorder, and persistent postconcussive symptoms in OIF/OEF veterans: polytrauma clinical triad. *J Rehabil Res Dev.* 2009; 46(6):697–702. [PubMed: 20104399]
22. Melzack R. The short-form McGill Pain Questionnaire. *Pain.* 1987; 30(2):191–7. [PubMed: 3670870]
23. Moeller-Bertram T, Afari N, Mostoufi S, Fink DS, Johnson Wright L, Baker DG. Specific pain complaints in Iraq and Afghanistan veterans screening positive for post-traumatic stress disorder. *Psychosomatics.* 2013 Mar 6. Epub ahead of print.
24. Muthen, LK.; Muthen, BO. *MPlus User's Guide*. Sixth. Los Angeles: Muthen & Muthen; 1998-2010.
25. National Center for PTSD. US Department of Veterans Affairs; 2012. Using the PTSD Checklist (PCL)
26. Outcalt SD, Yu Z, Hoen HM, Pennington TM, Krebs EE. Health care utilization among veterans with pain and posttraumatic stress symptoms. *Pain Med.* 2013 Feb 22. Epub ahead of print.
27. Palyo SA, Beck JG. Post-traumatic stress disorder symptoms, pain, and perceived life control: Associations with psychosocial and physical functioning. *Pain.* 2005; 117(1):121–7. [PubMed: 16099099]

28. Perilla JL, Norris FH, Lavizzo EA. Ethnicity, culture, and disaster response: identifying and explaining ethnic differences in PTSD six months after Hurricane Andrew. *J Soc Clin Psychol.* 2002; 21(1):20–45.
29. Perkins FM, Kehlet H. Chronic pain as an outcome of surgery: a review of predictive factors. *Anesthesiology.* 2000; 93(4):1123–33. [PubMed: 11020770]
30. Pietrzak RH, Goldstein RB, Southwick SM, Grant BF. Prevalence and Axis I comorbidity of full and partial posttraumatic stress disorder in the United States: results from Wave 2 of the National Epidemiologic Survey on Alcohol and Related Conditions. *J Anxiety Disord.* 2011; 25(3):456–65. [PubMed: 21168991]
31. Rahim-Williams FB, Riley JL III, Herrera D, Campbell CM, Hastie BA, Fillingim RB. Ethnic identity predicts experimental pain sensitivity in African Americans and Hispanics. *Pain.* 2007; 129(1):177–84. [PubMed: 17296267]
32. Ramchand R, Schell TL, Karney BR, Osilla KC, Burns RM, Caldarone LB. Disparate prevalence estimates of PTSD among service members who served in Iraq and Afghanistan: possible explanations. *J Trauma Stress.* 2010; 23(1):59–68. [PubMed: 20135699]
33. Resnick HS, Kilpatrick DG, Dansky BS, Saunders BE, Best CL. Prevalence of civilian trauma and posttraumatic stress disorder in a representative national sample of women. *J Consult Clin Psychol.* 1993; 61:984–91. [PubMed: 8113499]
34. Richards J, Meredith R, Nepomuceno C, Fine P, Bennett G. Psychosocial aspects of chronic pain in spinal cord injury. *Pain.* 1980; 8(3):355–66. [PubMed: 7402693]
35. Sayer NA, Rettmann NA, Carlson KF, Bernardy N, Sigford BJ, Hamblen JL, Friedman MJ. Veterans with history of mild traumatic brain injury and posttraumatic stress disorder: challenges from provider perspective. *J Rehabil Res Dev.* 2009; 46(6):703–16. [PubMed: 20104400]
36. Scherer M, Burrows H, Pinto R, Somrack E. Characterizing self-reported dizziness and otovestibular impairment among blast-injured traumatic amputees: a pilot study. *Mil Med.* 2007; 172(7):731–7. [PubMed: 17691686]
37. Schwarz GE. Estimating the dimension of a model. *Ann Stat.* 1978; 6(2):461–4.
38. Sharp TJ, Harvey AG. Chronic pain and posttraumatic stress disorder: mutual maintenance? *Clin Psychol Rev.* 2001; 21(6):857–77. [PubMed: 11497210]
39. Shipherd JC, Keyes M, Jovanovic T, Ready DJ, Baltzell D, Worley V, Gordon-Brown V, Hayslett C, Duncan E. Veterans seeking treatment for posttraumatic stress disorder: what about comorbid chronic pain? *J Rehabil Res Dev.* 2007; 44(2):153–66. [PubMed: 17551870]
40. Sledjeski E, Speisman B, Dierker L. Does the number of lifetime traumas explain the relationship between PTSD and chronic medical conditions? Answers from the National Comorbidity Survey-República (NCS-R). *J Behav Med.* 2008; 31:341–9. [PubMed: 18553129]
41. Sterling M, Jull G, Vicenzino B, Kenardy J, Darnell R. Physical and psychological factors predict outcome following whiplash injury. *Pain.* 2005; 114(1):141–8. [PubMed: 15733639]
42. Taylor BC, Hagel EM, Carlson KF, Cifu DX, Cutting A, Bidelsbach DE, Sayer NA. Prevalence and costs of co-occurring traumatic brain injury with and without psychiatric disturbance and pain among Afghanistan and Iraq War veteran VA users. *Med Care.* 2012; 50(4):342–6. [PubMed: 22228249]
43. Ullrich PM, Lincoln RK, Tackett MJ, Miskevics S, Smith BM, Weaver FM. Pain, depression, and health care utilization over time after spinal cord injury. *Rehabil Psychol.* 2013; 58(2):158–65. [PubMed: 23713727]
44. Villano C, Rosenblum A, Magura S, Fong C, Cleland C, Betzler T. Prevalence and correlates of posttraumatic stress disorder and chronic severe pain in psychiatric outpatients. *J Rehabil Res Dev.* 2007; 44(2):167. [PubMed: 17551871]
45. Walker WC, McDonald SD, Ketchum JM, Nichols M, Cifu DX. Identification of transient altered consciousness induced by military-related blast exposure and its relation to postconcussion symptoms. *J Head Trauma Rehabil.* 2013; 28(1):68–76. [PubMed: 22647964]
46. Weathers FW, Litz BT, Herman DS, Huska JA, Keane TM. The PTSD Checklist (PCL): Reliability, validity, and diagnostic utility. Proceedings of the 9th Annual Meeting of the International Society for Traumatic Stress Studies. 1993

Figure 1. Best-fitting autoregressive cross-lagged model with covariates included

Notes: Solid lines represent significant ($p < .05$) standardized regression estimates. Broken lines represent paths that were included in the model but were not statistically significant. PTSD= posttraumatic stress disorder; TBI= traumatic brain injury; AA= African-American. Only the statistically significant pathways for the covariates of age, race, and TBI injury status are illustrated in this figure.

Table 1

Descriptive characteristics of the sample.

	N	%
<i>Sex</i>		
Male	202	96.7
Female	7	3.3
<i>Race</i>		
White/Caucasian	164	78.5
African American	32	15.3
Other Race	13	6.2
<i>Deployment Location^a</i>		
Operation Enduring Freedom		
1 deployment	119	
2 deployments	31	
Operation Iraqi Freedom		
1 deployment	71	
2 deployments	29	
3 or more deployments	10	
Other Deployment Location	33	
<i>Branch of Service^a</i>		
Army	88	
Navy	4	
Air Force	2	
Marines	117	

Note:

^aSome participants endorsed more than one response.

Table 2

Correlations between age, posttraumatic stress disorder, and pain variables.

	M (SD)	1.	2.	3.	4.	5.	6.	7.
1. Age	27.4 (7.6)	-						
2. PCL Baseline (<i>n</i> = 209)	47.7 (14.9)	.22**	-					
3. PCL 6-Months (<i>n</i> = 126)	47.0 (17.9)	.18**	.65**	-				
4. PCL 12-Months (<i>n</i> = 112)	43.9 (16.8)	.40**	.63**	.85**	-			
5. SF-MPQ Baseline (<i>n</i> = 209)	11.0 (7.9)	.29**	.48**	.41**	.40**	-		
6. SF-MPQ 6-Months (<i>n</i> = 126)	11.8 (8.7)	.25**	.42**	.71**	.65**	.58**	-	
7. SF-MPQ 12-Months (<i>n</i> = 112)	11.5 (8.9)	.38**	.39**	.54**	.64**	.45**	.52**	-

Notes: PCL = Posttraumatic Stress Disorder Checklist; SF-MPQ = Short Form McGill Pain Questionnaire;

**

p < 0.001

Table 3

Best-fitting autoregressive simplex and autoregressive cross-lagged models examining the longitudinal relationships between pain and posttraumatic stress disorder symptoms over a one-year assessment period.

	χ^2	df	p	CFI	TLI	RMSEA (90% CI)	BIC	fp
Pain simplex	4.62	1	0.03	0.95	0.85	0.15 (0.04 – 0.31)	1650.08	6
PTSD simplex	0.20	1	0.66	1.00	1.02	0.00 (0.00 – 0.16)	1868.29	6
Cross-lagged, combined pain and PTSD ^a	2.80	3	0.42	1.00	1.00	0.00 (0.00 – 0.11)	6606.96	24
Cross-lagged, combined pain and PTSD with covariates added ^{a, b}	3.66	3	0.30	1.00	0.98	0.03 (0.00 – 0.13)	6678.31	54

Notes. PTSD = posttraumatic stress disorder; df = degrees of freedom; CFI = comparative fit index; TLI = Tucker-Lewis index; RMSEA = root mean squared error of approximation; BIC = Bayesian Information Criteria; fp = number of free parameters.

^aCross-lagged models combined pain and PTSD simplex models.

^bCovariates included age, race, and traumatic brain injury severity