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TITLE: Telephone-Delivered Cognitive Behavioral Therapy for Chronic Pain Following Traumatic Brain Injury

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14. ABSTRACT The purpose of this study is to evaluate the efficacy of a telephone-delivered cognitive behavioral treatment (T-CBT) in Veterans with a history of traumatic brain injury (TBI) for the treatment of chronic pain in a randomized controlled trial (RCT). Specifically, the RCT will examine the immediate (at the end of treatment) and long-term (6-months from randomization) efficacy of T-CBT on average pain intensity (primary outcome), and pain interference, sleep, depression, global impression of change, and life satisfaction (secondary outcomes) relative to a telephone-delivered pain psycho-educational active control condition (T-Ed) designed to control for time, dose, attention, and other nonspecific therapeutic effects such as therapeutic alliance. The study uses a 2-group parallel design. The sample will include 160 OEF/OIF Veterans with a history of TBI and chronic pain recruited from the VA Puget Sound Health Care System (VAPSHCS). Recruitment and enrollment for the study has not begun yet due primarily to unexpected delays in obtaining IRB approval from VAPSHCS, the study's primary recruitment site. The Human Research Protocol Submission Form for this study was submitted to the Human Research Protections Office (HRPO) August 8 th , 2013 and is still pending approval.					
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Introduction

The purpose of this study is to evaluate the efficacy of a telephone-delivered cognitive behavioral treatment (T-CBT) in Veterans with a history of traumatic brain injury (TBI) for the treatment of chronic pain in a randomized controlled trial (RCT). Specifically, the RCT will examine the immediate (at the end of treatment) and long-term (6-months from randomization) efficacy of T-CBT on average pain intensity (primary outcome), and pain interference, sleep, depression, global impression of change, and life satisfaction (secondary outcomes) relative to a telephone-delivered pain psycho-educational active control condition (T-Ed) designed to control for time, dose, attention, and other nonspecific therapeutic effects such as therapeutic alliance. The study uses a 2-group parallel design. The sample will include 160 OEF/OIF Veterans with a history of TBI and chronic pain recruited from the VA Puget Sound Health Care System (VAPSHCS).

Body

Development:

The study received full approval from both the Veterans Affairs Puget Sound Health Care System's (VAPSHCS) Research and Development Committee and Institutional Review Board (IRB) August 22, 2013. Study personnel received full approval from the University of Washington's (UW) IRB March 25, 2013. Study personnel submitted the VA approved IRB materials from both institutions to the US Army Medical Research and Materiel Command (USAMRMC) Office of Research Protections (ORP) Human Research Protections Office (HRPO) on August 8, 2013. We anticipate that the study will receive full HRPO IRB approval in November 2013.

The study PI has convened study meetings with study investigators on a bi-weekly basis as well as weekly meetings with the PI, the VA PI and key staff members to attend to pertinent development and preparation topics throughout Year 1. We have constructed and tested databases for session data and tracking. In addition, study personnel have finalized recruitment, enrollment and randomization procedures.

We determined that a subcontract with the VA was needed to hire appropriate study personnel and was agreed to by all parties. A revised budget and subcontract budget were submitted to and approved by the CDMRP.

Preparation:

Study personnel have obtained a Certificate of Confidentiality (CoC) from the National Institutes of Health (NIH). In addition, study personnel are finalizing study treatment manuals and participant workbooks. Study personnel have purchased all major supplies for the study. The VAPSHCS research coordinator and assistant have been trained in study procedures. Study personnel have also opened a checking account for human subject payments as well as acquired cell phone plans that will be used by study clinicians during treatment.

Formative Evaluation:

The study PI and VA PI have met with VAPSHCS medical providers to strategize the implementation of advisory group meetings with both providers and VA patients. The dual purpose of these meetings will be a) to collect data regarding current practice of pain treatment and b) identify current barriers to treatment for the study population.

Problems Encountered:

Considerable effort and time were expended to submit the VA IRB application. The length of time required to submit the application has caused a delay in subject recruitment and enrollment by approximately 1-2 months. In addition, it took the VAPSHCS IRB committee a considerable amount of time to review the application; study personnel submitted the application in early January, with final approval taking place August 22, 2013. We anticipate that the length of time the VAPSHCS IRB reviewed the application (almost eight months) may cause a potential delay in subject recruitment and enrollment by an additional 3-4 months.

We believe we will still be able to achieve our enrollment goals despite these delays given a) the research team consists of members with extensive experience in subject recruitment, b) the expressed commitment by VAPSHCS providers to help study personnel achieve their recruitment goals, and 3) the large number of patients within the VAPSHCS that we project to be eligible and willing to participate.

Key Research Accomplishments

Recruitment, enrollment and data collection have not commenced yet given the delays in obtaining full IRB approval from all responsible institutions.

Given that the study materials have been prepared, we are using our study clinician time to assist in producing possible publications from existing data on TBI and subsequently relevant to the current study.

Reportable Outcomes

As mentioned above, recruitment, enrollment and data collection have not commenced yet given the delays in obtaining full IRB approval from all responsible institutions.

We have submitted one paper based on previously collected data, but relevant to our current study:

Sullivan-Singh, S, Sawyer, K, Ehde, D, Bell, K, Temkin, N, Dikmen, S, Williams, R, & Hoffman, J. Comorbidity of pain and depression among persons with traumatic brain injury. Archives of Physical Medicine and Rehabilitation.

Abstract

Objective: To assess the prevalence of pain, depression, and comorbid pain and depression among a civilian sample of persons with traumatic brain injury (TBI).

Research Method/Design: Longitudinal survey design with 1-year follow up. Setting: Data were collected during inpatient rehabilitation and in the community at one year after injury.

Participants: The participants were 158 persons admitted to inpatient rehabilitation following moderate to severe TBI. Interventions: Not applicable. Main Outcome *Measures:* Depression was assessed with the Patient Health Questionnaire (PHQ-9); pain was assessed with a numerical rating scale (0= no pain to 10= worst pain); participants who reported average pain ≥ 4 were classified as having pain and participants with PHQ-9 scores ≥ 10 were classified as depressed.

Results: Both pain and depression were more prevalent at baseline assessment (pain: 70%; depression: 31%) than at year 1 (pain: 34%; depression: 22%). Comorbid pain and depression declined from 27% at baseline to 18% at year 1. Pain was significantly associated with depression at baseline (RR: 2.62, $p = .003$) and at year1 (RR: 7.98, $p < .001$).

Conclusions/Implications: Pain and depression are common and frequently co-occur in persons with TBI. Whereas their frequency declined over the first year following injury, the strength of their association increased. Assessment and treatment of both conditions simultaneously may lead to improved outcomes, both early after TBI as well as over time.

See appendices for full manuscript.

Conclusion

We plan to make the following progress in the 1st quarter of the 2nd year of this research study.

Development:

Study personnel plan to obtain USAMRMC HRPO approval to engage in human subjects research during the next reporting period. Study investigators and study personnel will continue to meet on a regular basis to discuss pertinent matters including recruitment and enrollment strategies.

Preparation:

Study personnel will order study materials including treatment workbooks from UW Publication Services. Finally, study personnel will implement a 'Kick-Off' meeting once recruitment and enrollment begins.

Participant Enrollment/Data Acquisition:

Study personnel will begin to recruit and enroll an average of about 6-8 subjects per month with recruitment and enrollment planned to start in Month 14. Study personnel will also commence random assignment of subjects to treatment intervention, and conduct treatment with subjects. Further, study personnel will begin collecting study data from subjects both in-person and via telephone. The study PI and investigators will provide ongoing supervision to research and clinical staff, as well as facilitate regular meetings with research staff and investigators to address enrollment issues.

Operations and Maintenance:

Dr. Hoffman, Dr. Williams and Mr. Gertz will monitor study personnel performance to ensure adherence to procedures.

In addition, Drs. Hoffman and Ehde will commence weekly meetings with study clinicians to address any clinical issues that may arise during treatment.

Data Management and Analysis:

Study personnel will complete database development as well as commence data entry and routine data checking.

Formative Evaluation:

The study PI and study personnel will consult with the Polytrauma and Blast-Related Quality Enhancement Research Initiative (QUERI) group and Tele-mental Health at VAPSHCS to assess important factors related to implementation. Further, study personnel will conduct advisory group meetings with both providers and VA patients to collect data regarding current practice of pain treatment and identify current barriers to treatment for the study population.

References

There are no references pertinent to this report.

Appendices

We have submitted one paper based on previously collected data, but relevant to our current study:

Sullivan-Singh, S, Sawyer, K, Ehde, D, Bell, K, Temkin, N, Dikmen, S, Williams, R, & Hoffman, J. Comorbidity of pain and depression among persons with traumatic brain injury. Archives of Physical Medicine and Rehabilitation.

We have also included a Quad Chart for this particular study as requested by the CDMRP.

Telephone-Delivered Cognitive Behavioral Therapy for Chronic Pain Following Traumatic Brain Injury



PI: Jeanne M. Hoffman, Ph.D.

Org: University of Washington

Award Amount: \$3,085,185

Log#: PT110602, Applied Neurotrauma Research Award with Clinical Trial

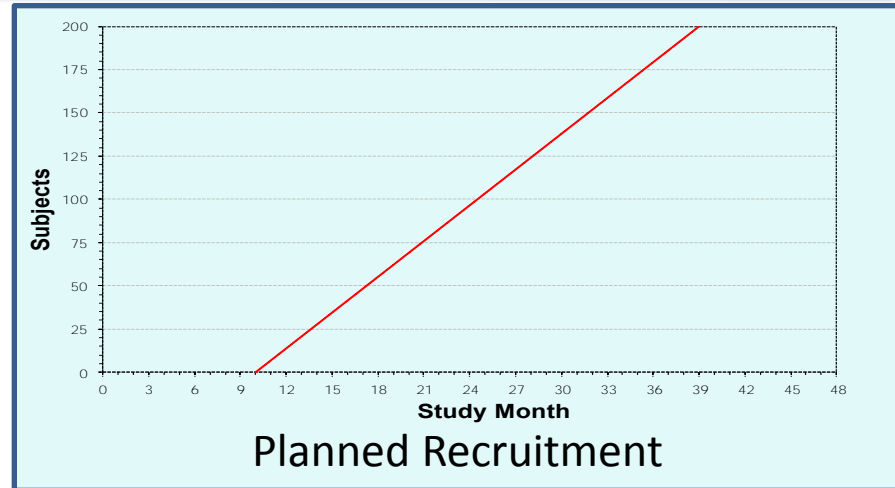
Award # W81XWH-12-2-0109

Study/Product Aim(s)

- We will evaluate the efficacy of telephone-delivered cognitive behavioral therapy (T-CBT) for reducing average pain intensity relative to telephone-delivered education intervention (T-Ed) in Veterans with a history of TBI.
- We will determine the efficacy of T-CBT relative to T-Ed in reducing pain interference, sleep problems, and depression, as well as improving global impression of change and life satisfaction.
- We will determine whether treatment effects are maintained 6 months after randomization.
- We will conduct a formative evaluation to identify key factors relevant to future dissemination and implementation of the intervention into the VA.

Approach

The sample will include 160 OEF/OIF/OND Veterans with a history of TBI and chronic pain recruited from the VA Puget Sound Health Care System (VAPSHCS). Participants will be randomized to either T-CBT or T-Ed (2 group parallel design). Each treatment will consist of eight 60-minute sessions conducted over the telephone over 8-12 weeks. Information about pain and the other commonly co-occurring conditions described above will be collected before, mid treatment, post treatment and at 6 months following randomization.



Accomplishment: Investigators have accomplished almost all preparation and development components except receipt of full IRB approval. We anticipate beginning participant recruitment and enrollment in Month 14.

Timeline and Cost

Activities	CY	13	14	15	16
IRB approval, finalize protocol, intervention manual, develop databases		█			
Participant Enrollment/Data Acquisition			█	█	█
Formative Evaluation		█	█	█	█
Publication/Dissemination					█
Estimated Total Budget (\$K)		\$666	\$874	\$889	\$656

Goals/Milestones

CY13 Goal – Development and Preparation

- IRB approval
- Finalize study protocol, intervention manual, databases

CY14 Goals – Participant Enrollment/ Data Acquisition

- Enroll 75 subjects
- Assess important factors contribute formative evaluation

CY15 Goal – Participant Enrollment/ Formative Evaluation

- Enroll 100 subjects
- Collect data current practice-formative evaluation

CY16 Goal – Participant Enrollment/ Formative Evaluation/Dissemination

- Complete enrollment and data acquisition (total of 200 enrolled subjects)
- Produce manual and training program- formative evaluation
- Disseminate study findings in primary paper

Comments/Challenges/Issues/Concerns

- Participant enrollment delayed 4-6 months by prolonged IRB approval process.

Budget Expenditure to Date (Through 30/09/2013)

Projected Expenditure: \$666,320

Actual Expenditure: \$590,880

Updated: 25/10/2013

Comorbidity of Pain and Depression Among Persons with Traumatic Brain Injury

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Sources of Support: This research was supported by the National Institute on Disability and Rehabilitation Research Traumatic Brain Injury Model Systems (grant no. H133A070032) and Department of Defense Congressionally Directed Medical Research Programs (grant no. W81XWH-12-2-0109).

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We certify that no party having a direct interest in the results of the research supporting this article has or will confer a benefit on us or on any organization with which we are associated,

and we certify that all financial and material support for this research and work are clearly identified in the title page of the manuscript: Sarah J. Sullivan-Singh, Kate Sawyer, Dawn M. Ehde, Kathleen R. Bell, Nancy Temkin, Sureyya Dikmen, Rhonda M. Williams, Jeanne M. Hoffman.

Abstract

Objective: To assess the prevalence of pain, depression, and comorbid pain and depression among a civilian sample of persons with traumatic brain injury (TBI).

Research Method/Design: A longitudinal survey design.

Setting: Data were collected during inpatient rehabilitation and in the community at one year after injury.

Participants: The participants were 158 persons admitted to inpatient rehabilitation and enrolled in the University of Washington TBI Model System.

Interventions: Not applicable.

Main Outcome Measures: Depression was assessed with the Patient Health Questionnaire (PHQ-9); pain was assessed with a numerical rating scale (0= no pain to 10= worst pain); participants who reported average pain ≥ 4 were classified as having pain and participants with PHQ-9 scores ≥ 10 were classified as depressed.

Results: Both pain and depression were more prevalent at baseline assessment (pain: 70%; depression: 31%) than at year 1 (pain: 34%; depression: 22%). Comorbid pain and depression declined from 27% at baseline to 18% at year 1. Pain was significantly associated with depression at baseline (RR: 2.62, $p = .003$) and at year1 (RR: 7.98, $p < .001$).

Conclusions/Implications: Pain and depression are common and frequently co-occur in persons with TBI. Whereas their frequency declined over the first year following injury, the strength of their association increased. Assessment and treatment of both conditions simultaneously may lead to improved outcomes, both early after TBI as well as over time.

Key Words: pain, depression, TBI.

Abbreviations: APS = analog pain scale; CI: confidence interval; GCS = Glasgow Coma Scale; M = arithmetic mean; OR = odds ratio; PHQ-9 = 9-item Patient Health Questionnaire; RR = relative risk; TBI = traumatic brain injury; TBIMS = Traumatic Brain Injury Model Systems;

Both pain and depression are common among persons who have experienced moderate to severe traumatic brain injury (TBI). Estimated rates of major depressive disorder in the year following TBI range from 26 to 53%,¹⁻³ which stands in contrast to a 12-month prevalence of 6.7% in the general adult population.⁴ Likewise, while prevalence estimates of chronic pain vary depending on how pain is assessed, there is evidence that chronic pain may be more prevalent among persons with history of TBI than the general population. A review of 23 studies examining chronic pain after TBI suggested a point prevalence of 57.8% (95% CI: 55.5%-60.2%) for chronic headaches when combining civilian and military samples.⁵ The same review estimated a prevalence of 51.5% for general chronic pain among civilian (i.e., non-military) persons who have experienced TBI. The prevalence of chronic pain is somewhat lower in the general adult population, ranging from 37 to 43%.^{6,7} Although persons with a history of moderate to severe TBI appear to bear an increased burden of both depressive symptoms and chronic pain relative to the general populations, there is little research examining the co-occurrence of depression and pain in this population.

Existing literature on depression and pain in the general population as well as in other neurological groups (e.g., multiple sclerosis⁸), documents significant comorbidity between these conditions.^{9,10} This co-occurrence may result because depression and chronic pain interact so as to exacerbate each other.⁹ Investigators have proposed a variety of causal mechanisms for this reciprocal relationship. A recent review summarized these potential mechanisms, including: shared neurotransmitter pathways; mutual impact on cognitive processes such as threat appraisal and catastrophizing; and a cycle of behavioral changes, including reduced activity and subsequent increases in pain and depressive symptoms.¹⁰ Some researchers have even suggested that the presence of both pain and depression might be more accurately conceptualized as a

“depression-pain syndrome” rather than the presence of two independent disorders.¹¹ In addition to possible shared etiology, there is also evidence that the co-occurrence of pain and depression is clinically significant. For instance, the extant literature suggests that persons with both chronic pain and depression experience greater disability than do persons with only chronic pain or depression.^{10,12} Their comorbidity also has implications for treatment: research in other populations has shown that both conditions may reduce treatment responsiveness in the other condition.^{10,13–15}

While evidence exists that both chronic pain and depression are common among persons with history of TBI and that the co-occurrence of pain and depression is clinically important, we are not aware of any studies examining the comorbidity of pain and depression among persons with history of TBI. A recent systematic review of studies investigating pain among persons with TBI reported that “low grade” evidence exists for an association between depression and pain in persons with TBI.¹⁶ If it were the case that pain and depression occur relatively independently of each other among persons with TBI, it would follow that pain and depression are separate constructs that can be assessed and treated independently in this population. Conversely, evidence of pain and depression being highly comorbid in persons with TBI would suggest that the interplay of pain and depression is similar to that observed in the general population. Such findings would highlight the importance of further research examining how best to assess and treat both conditions in this population.

To investigate these questions, we examined the co-occurrence of pain and depression in a cohort of participants with moderate to severe TBI both during inpatient rehabilitation and at 1-year post injury. Given that the first year after TBI is typically an active time of recovery and change in functioning, we were interested in exploring whether and how the frequency of, and

association between, pain and depression might change over time. Based on existing literature, our hypotheses were that, at both time points, persons with pain would be more likely to be depressed and persons with depression would be more likely to have pain.

Methods

Subjects

Participants were part of a larger study of individuals enrolled into the University of Washington Traumatic Brain Injury Model System (TBIMS). The TBIMS is a longitudinal study sponsored by the National Institute on Disability and Rehabilitation Research. Inclusion criteria for the TBIMS are 1) diagnosis of TBI by either Glasgow Coma Scale (GCS)¹⁷ score <13 on emergency department admission; >30 minutes of loss of consciousness; >24 hours post traumatic amnesia, or neuroimaging indicating intracranial abnormality; 2) ≥ 16 years of age; 3) admission to the acute hospital within 72 hours of injury; and 4) receipt of both medical and rehabilitation care within the same system. Over 90% of eligible subjects during this study period consented to enrollment in the TBIMS and completed in-person assessment during inpatient rehabilitation (baseline); over 90% of those enrolled completed assessment by telephone at one-year post injury (year 1). In addition to the data collected for the TBIMS, participants were also asked about their pain and mood at baseline and 1-year post injury. Of the 174 individuals who were consecutively enrolled between August 2004 and October 2007, 158 completed the measures of pain and depression at baseline and 116 completed them at 1-year post injury. Of the 42 participants for whom year 1 data were not available, only 15 were lost to follow up. The remaining 27 participants were unable to complete the specific measures necessary for the current analyses due to time constraints. Data from this study have been previously used to describe sleep and co-occurring psychological conditions after TBI,¹⁸ but the

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data utilized for the analyses that follow have not been previously reported. All study procedures for the TBIMS and additional measures were approved by the University of Washington Human Subjects Review Committee, and informed consent was obtained from each participant.

Measures

Pain: 0-10 Numeric Rating Scale. Participants were asked to rate their overall pain, acknowledging that they may have pain in multiple locations using the Analog Pain Scale. Three questions about pain were asked: 1) overall average intensity of pain during the past week 2) worst pain over the past week, and 3) current pain on a 0 - 10 Numerical Rating Scale (NRS), with 0 = “No pain” and 10 = “Pain as bad as could be.” These ratings were averaged to create a “characteristic pain score” that has been shown to be a valid and reliable measure of pain intensity.^{19,20} In the present study, and consistent with research on persons with other types of pain,²¹⁻²³ participants with an average score of ≥ 4 were considered to have at least moderate pain..

Depression: Patient Health Questionnaire-9 (PHQ-9). The PHQ-9 is a commonly used measure of depression in medical populations²⁴ and has been validated in TBI populations.²⁵ Consistent with published guidelines, in the present study, participants who scored ≥ 10 were classified as “depressed.”²⁵

Data analysis

Using the cutoffs for pain and depression described above, descriptive statistics were computed to identify frequencies of pain alone, depression alone, comorbid pain and depression, and neither pain nor depression at both baseline and year 1. A Fisher Exact test was conducted for each time point to test for associations between pain and depression. We also calculated the relative risk that (a) a participant with depression would have pain relative to a participant

without depression and (b) a participant with pain would have depression relative to a participant without pain. Finally, for the 116 participants for whom both pain and depression data were available at both time points, we conducted a subgroup analysis investigating the frequency of pain and depression at year 1 within each of the four baseline depression/pain status categories.

Results

Demographics

Demographic and injury characteristics of the sample at baseline ($N = 158$) and year 1 ($N = 116$) are displayed in Table 1. Of note, complete data on pain and depression were available for only 73% of participants at year 1. Participants who did not complete the year 1 assessment had received, on average, fewer years of education, were more likely to be of non-Caucasian race, and were less likely to have been competitively employed prior to injury. Importantly, there were no significant differences on baseline rates of pain and depression between participants who completed all measures at year 1 and those who did not.

Depression & Pain

Table 2 displays the prevalence of pain, depression, and the co-occurrence of pain and depression at baseline and year 1. The majority of participants (70%) reported experiencing at least moderate pain at baseline (> 4). Notably, the proportion of participants reporting at least moderate pain decreased to 34% at year 1. At both time points, depression was somewhat less prevalent in comparison to pain, with 31% of participants reporting depression at baseline and only 22% at year 1. The proportion of participants reporting comorbid pain and depression also decreased over time from 27% at baseline to 18% at year 1. These decreases in participants reporting depression and pain across time corresponded to a large increase in the proportion of participants reporting neither pain nor depression at Year 1.

Relative risk was calculated at each time point to examine the possibility that being classified as having pain might confer an increased likelihood of being classified as having depression and vice versa. A Fisher Exact test was conducted to test the significance of these associations. As shown in Table 2, at baseline there was a statistically significant relationship between pain and depression: participants who reported pain were 1.37 times more likely to report depression and participants who reported depression were 2.62 times more likely to report pain ($p < .003$). The magnitude of this association was larger at year 1: participants who reported pain were 3.83 times more likely to report depression and participants who reported depression were 7.98 times more likely to report pain ($p < .001$)

Table 3 illustrates pain and depression outcomes at year 1 as a function of pain and depression status at baseline (the 116 participants who had data for all critical variables at both time periods were included). Because only three participants were in the Depression Only group at baseline, it is difficult to interpret the meaning of their trajectory over time. With regard to the other groups, the majority of each group moved to having neither condition at year 1 or stayed within the same category. A small percentage got worse (moving to the Depression & Pain group) or, in the case of those who were in the Neither group at baseline, developed pain or depression.

Discussion

Consistent with literature in other populations, pain and depression were common among individuals with TBI. Although their prevalence diminished over time, the conditions co-occurred at both time points. Furthermore, the strength of their association increased over the follow-up period. While most individuals improved over time, a larger fraction of those who had pain or pain and depression were still suffering with one or both conditions at year 1.

The current findings are generally consistent with the extant literature on the comorbidity of pain and depression in the general population. This literature suggests that the conditions are often comorbid but that they are also independent problems with many persons suffering from just one or the other condition.⁹ Hence, it is important for clinicians to be aware of potential comorbidity in persons with TBI and to carefully assess for depression when pain is present and vice versa. Existing research in the general population underscores the need to coordinate identification and management of these two conditions given their high comorbidity and the potential risk of failing to recognize depression as a possible contributor to somatic symptoms (e.g., fatigue, insomnia) that persons with pain (and TBI) often report.¹⁰ The current results point to the highest incidence of comorbid depression and pain occurring early on in the course of recovery from TBI. However, although the proportion of persons suffering from both conditions declined between assessments, the linkage between the conditions actually grew over time. These findings highlight the importance of assessing pain and depression on repeated occasions over the course of recovery from TBI in both clinical and research settings.

In light of the current results, further research investigating the potential mechanisms (e.g., behavioral, cognitive, neurophysiological) underlying this comorbidity among persons with TBI is warranted. Future research may benefit from measuring both depression and pain repeatedly over time to examine their reciprocal relationship and determine whether changes in one variable are predictive of changes in the other. One study that examined the reciprocal relationship between depression and functional limitations following TBI found that functional limitations predicted depression over time whereas depression did not predict functional limitations over time, suggesting that treating functional limitations may be paramount for addressing depression in persons with TBI.²⁶ If such a pattern were revealed between pain and depression over time

among persons with TBI, it would be critical in guiding treatment recommendations and planning. It may also prove fruitful to explore trajectories or classes of people who respond more and less positively to treatment for pain, depression, and pain and depression combined so that increasingly targeted treatments can be developed and the effective allocation of treatment resources can be maximized.

Limitations

Given that the sample was drawn from one treatment center and was relatively homogenous with regard to ethnic composition, there are possible limitations to generalizability of the results. In addition, all participants had suffered recent injuries, received inpatient rehab, and received treatment in an academic medical center, which may mean participants received a different level of inpatient care and outpatient follow up care than would be available in many areas. Finally, those subjects who did not complete all measures at one year may have experienced additional psychosocial difficulties which could lead to an underestimation of pain and depression at that time period.

Conclusions

Despite these limitations, the current research provides critical data regarding the prevalence of pain and depression and their comorbidity among persons with TBI. The results indicate that the conditions are both prevalent and often comorbid. However, while the prevalence of both conditions diminished over the follow-up period, the association between the two conditions actually became stronger over time, suggesting that it is essential to be aware of potential comorbidity throughout the course of recovery from TBI. Future research will be essential for developing an increasingly nuanced understanding of the interplay of these conditions over time and their impact on treatment outcomes.

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References

1. Hart T, Brenner L, Clark AN, Bogner JA, Novack TA, Chervoneva I, et al. Major and minor depression after traumatic brain injury. *Arch Phys Med Rehabil.* 2011;92:1211–9.
2. Gould KR, Ponsford JL, Johnston L, Schönberger M. The nature, frequency and course of psychiatric disorders in the first year after traumatic brain injury: a prospective study. *Psychol Med.* 2011;41:2099–109.
3. Bombardier C, Fann J. Rates of major depressive disorder and clinical outcomes following traumatic brain injury. *JAMA.* 2010;303:1938–45.
4. Kessler R, Chiu W. Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry.* 2005;62:617–27.
5. Nampiaparampil D. Prevalence of Chronic Pain After Traumatic Brain Injury. *JAMA.* 2008;300:711–9.
6. Tsang A, Von Korff M, Lee S, Alonso J, Karam E, Angermeyer MC, et al. Common chronic pain conditions in developed and developing countries: gender and age differences and comorbidity with depression-anxiety disorders. *J Pain.* 2008;9:883–91.
7. CDC, NCHS (National Center for Health Statistics). *Health, United States, 2010, chartbook, special feature on death and dying.* Hyattsville, MD: 2010.
8. Alschuler KN, Ehde DM, Jensen MP. The co-occurrence of pain and depression in adults with multiple sclerosis. *Rehabil Psychol.* 2013;58:217–21.
9. Kroenke K, Wu J, Bair MJ, Krebs EE, Damush TM, Tu W. Reciprocal relationship between pain and depression: a 12-month longitudinal analysis in primary care. *J Pain.* 2011;12:964–73.
10. Bair MJ, Robinson RL, Katon W, Kroenke K. Depression and Pain Comorbidity. *Arch Intern Med.* 2003;163:2433–45.
11. Lindsay P, Wyckoff M. The depression-pain syndrome and its response to antidepressants. *Psychosomatics.* 1981;22:571–3.
12. Ericsson M, Poston WSC, Linder J, Taylor JE, Haddock CK, Foreyt JP. Depression predicts disability in long-term chronic pain patients. *Disabil Rehabil.* 2002;24:334–40.
13. Kroenke K, Shen J, Oxman TE, Williams JW, Dietrich AJ. Impact of pain on the outcomes of depression treatment: Results from the RESPECT trial. *Pain.* 2008;134:209–15.

14. Mavandadi S, Ten Have TR, Katz IR, Durai UNB, Krahn DD, Llorente MD, et al. Effect of depression treatment on depressive symptoms in older adulthood: the moderating role of pain. *J Am Geriatr Soc.* 2007;55:202–11.
15. Miller LR, Cano A. Comorbid chronic pain and depression: who is at risk? *J Pain.* 2009;10:619–27.
16. Dobscha SK, Clark ME, Morasco BJ, Freeman M, Campbell R, Helfand M. Systematic review of the literature on pain in patients with polytrauma including traumatic brain injury. *Pain Med.* 2009;10:1200–17.
17. Wilson JT, Pettigrew LE, Teasdale GM. Structured interviews for the Glasgow Outcome Scale and the extended Glasgow Outcome Scale: guidelines for their use. *J Neurotrauma.* 1998;15:573–85.
18. Fogelberg DJ, Hoffman JM, Dikmen S, Temkin NR, Bell KR. Association of sleep and co-occurring psychological conditions at 1 year after traumatic brain injury. *Arch Phys Med Rehabil.* 2012;93:1313–8.
19. Jensen M, Karoly P. Self-report scales and procedures for assessing pain in adults. In: Turk DC, Melzack R, editors. *Handbook of pain assessment.* New York: 2001. p. 15–34.
20. Korff M Von, Ormel J, Keefe F, Dworkin S. Grading the severity of chronic pain. *Pain.* 1992;50:133–49.
21. Zelman DC, Dukes E, Brandenburg N, Bostrom A, Gore M. Identification of cut-points for mild, moderate and severe pain due to diabetic peripheral neuropathy. *Pain.* 2005;115:29–36.
22. Fejer R, Jordan A, Hartvigsen J. Categorising the severity of neck pain: establishment of cut-points for use in clinical and epidemiological research. *Pain.* 2005;119:176–82.
23. Tan G, Jensen MP, Thornby JI, Rintala DH, Anderson KO. Categorizing pain in patients seen in a veterans health administration hospital: Pain as the fifth vital sign. *Psychol Serv.* 2008;5:239–50.
24. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med.* 2001;16:606–13.
25. Fann JR, Bombardier CH, Dikmen S, Esselman P, Warms C a, Pelzer E, et al. Validity of the Patient Health Questionnaire-9 in assessing depression following traumatic brain injury. *J Head Trauma Rehab.* 2005;20:501–11.
26. Pagulayan KF, Hoffman JM, Temkin NR, Machamer JE, Dikmen SS. Functional limitations and depression after traumatic brain injury: examination of the temporal relationship. *Arch Phys Med Rehabil.* 2008;89:1887–92.

Table 1. Baseline Measures: Comparing Study Completers and Non-Completers

	Total Sample <i>N</i> = 158	Study Completers <i>N</i> = 116	Incomplete Data/ Lost to Follow Up <i>N</i> = 42
	<i>M</i> or <i>N</i> (<i>SD</i> or %)	<i>M</i> or <i>N</i> (<i>SD</i> or %)	<i>M</i> or <i>N</i> (<i>SD</i> or %)
Age	37.5 (16.4)	36.6 (15.6)	40.1 (18.2)
Male	125 (80%)	92 (80%)	33 (79%)
Race*			
White	124 (79%)	98 (85%)	26 (62%)
Hispanic	15 (10%)	7 (6%)	8 (19%)
African American	13 (8%)	7 (6%)	6 (14%)
Asian/Pacific Islander	3 (2%)	2 (2%)	1 (2%)
Native American	2 (1%)	1 (1%)	1 (2%)
Unknown	1	1	0
Education*			
High school or above	114 (73%)	89 (77%)	25 (60%)
Less than high school	43 (27%)	26 (23%)	17 (40%)
Unknown	1	1	0
Married	72 (46%)	54 (47%)	18 (43%)
Employed prior to injury*	106 (68%)	84 (73%)	22 (52%)
Glasgow Coma Scale	8.6 (4.2)	8.9 (4.2)	8.0 (4.1)
Unknown	54	39	15
Cause of Injury			
Vehicular	83 (53%)	63 (55%)	20 (49%)
Fall	37 (24%)	27 (23%)	10 (24%)
Violence	13 (8%)	7 (6%)	6 (15%)
Other	23 (15%)	18 (16%)	5 (12%)
FIM™ score (discharge)	104 (14)	105 (14)	102 (16)
PHQ-9 score	7.4 (5.5)	6.9 (4.7)	8.8 (7.0)
Average pain	4.5 (2.5)	4.4 (2.4)	4.8 (2.7)

* Denotes a significant difference ($p < .05$) between participants for whom complete data were and were not available at year 1.

Depression Only	7 (4.43%)	5 (4.31%)
Pain & Depression	42 (26.58%)	21 (18.10%)
Neither	41 (25.95%)	71 (61.21%)
RR[‡] that depressed participant will have pain	2.62	7.98
RR[‡] that participant with pain will be depressed	1.37	3.83
Fisher Exact Significance	.003	<.001

* Pain defined as APS characteristic pain score ≥ 4

† Depression defined as PHQ-9 score ≥ 10 .

‡ Relative risk was computed to describe the likelihood that 1) a participant classified as having depression would also be classified as having pain (relative to a participant without depression), and b) a participant classified as having pain would also be classified as having depression (relative to a participant without pain).

Table 3: Percentage and frequency of participants* reporting pain, depression, both conditions, and neither condition at year 1, separated by depression and pain classification at baseline.

	<i>Baseline</i>			
	Pain Only (<i>n</i> = 53) 46%	Depression Only (<i>n</i> = 3) 3%	Pain & Depression (<i>n</i> = 29) 25%	Neither (<i>n</i> = 31) 27%
<i>Year 1</i>				
Pain Only	23% (12)	33% (1)	7% (2)	13% (4)
Depression Only	6% (3)	0% (0)	3% (1)	3% (1)
Pain & Depression	13% (7)	33% (1)	38% (11)	6% (2)
Neither	58% (31)	33% (1)	52% (15)	77% (24)

* Table contains only participants who had known values for both pain and depression measures at both time points (*N* = 116).