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Relationship between Extreme Pain Phenotypes and Psychosocial Outcomes in Persons with Chronic Pain following Traumatic Brain Injury: A NIDILRR and VA TBI Model Systems Collaborative Project

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Abstract

Objective: To examine the relationship between extreme pain phenotypes (interference and improvement) and psychosocial outcomes among those with chronic pain after traumatic brain injury (TBI).

Setting: Community.

Participants: 1,762 TBI Model Systems (TBIMS) participants 1-30 years post-injury reporting chronic pain.

Design: Multi-site, cross-sectional observational cohort study.

Primary Measure(s): Life satisfaction, post-traumatic stress, depression and anxiety symptoms, sleep and participation, Brief Pain Inventory (BPI) interference scale, Patients Global Impression of Change (PGIC).

Results: Persons in the extreme high interference phenotype (vs extreme low interference phenotype) and/or extreme no change phenotype (vs extreme improvement phenotype) had poorer psychosocial outcomes, with extreme pain interference phenotypes having a larger effect on outcomes than extreme perceived improvement phenotypes. After controlling for covariates, large effect sizes (ES) related to pain interference were observed for post-traumatic stress symptomology (ES = −1.14), sleep quality (ES = −1.10), depression (ES = −1.08), anxiety (ES = −0.82), and life satisfaction (ES = 0.76); effect sizes for participation outcomes, although significant, were relatively small (ES = 0.21-0.36). Effect sizes related to perceived improvement were small for life satisfaction (ES = 0.20) and participation (ES = 0.16-0.21) outcomes. Pain intensity was identified as a meaningful confounding factor of the relationships between extreme phenotypes and post-traumatic stress, depression, anxiety, and sleep quality.

Conclusions: Examination of extreme phenotypes provides important insights on the experience of individuals living with chronic pain and TBI. Results suggest that the relationships among a variety of characteristics of the person, their experience with pain, and treatment of pain is complex. Further research is needed to better understand these complex relationships and how differences in pain interference and perceived improvement from treatment can assist in assessment and treatment of chronic pain after TBI.

Keywords

Traumatic Brain Injury; Chronic Pain; Psychosocial Outcomes; Extreme Phenotypes

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INTRODUCTION

Psychosocial outcomes like satisfaction with life, community participation, symptoms of psychological distress, and sleep disturbance are important indicators of successful rehabilitation and functioning following traumatic brain injury (TBI). As a co-morbid condition, chronic pain (defined as pain lasting for at least three months),[1] has the potential to negatively impact psychosocial outcomes following TBI. For those with TBI, the prevalence of depression (21.0%) and anxiety disorders (19.5%) has been well-documented.[2] In the presence of experiencing pain, individuals with mild TBI reported more severe symptoms of depression and anxiety as compared to healthy controls,[3,4] and more severe and persistent chronic pain.[3,5] Additionally, posttraumatic stress disorder (PTSD) is one of the most commonly reported psychiatric disorders following TBI[6] among Veterans, with over half experiencing co-morbid chronic pain and PTSD.[7] This co-morbid constellation is so prevalent it is referred to as the “polytrauma clinical triad” among Veterans and Service Members of recent military conflicts.[8] Further, this triad is strongly associated with significant sleep disturbances, and shown to exacerbate chronic pain and worsen other conditions (e.g., depression, anxiety) following TBI.[9] Finally, findings generally support that chronic pain intertwined with other aforementioned psychological conditions (e.g., depression) can negatively impact more global outcomes like community participation and long-term life satisfaction following TBI.[10]

In our own observations within a large-scale sample of individuals with TBI,[11] we found that these psychosocial outcomes differ significantly between individuals with TBI reporting concurrent chronic pain compared to those who experienced either past or no chronic pain. Specifically, individuals with TBI currently experiencing chronic pain demonstrated the highest reported symptoms of post traumatic stress (PTS), anxiety, and depression, and the lowest levels of sleep quality, community participation, and satisfaction with life compared to individuals reporting either past or no chronic pain. However, the experience of chronic pain is highly variable, including the type of pain, but also the impact of pain on interference with daily activities or how someone may have benefited from treatment, even if still experiencing chronic pain. Research examining factors such as pain severity and interference in daily life has shown greater pain severity scores were associated with greater anxiety, and higher rates of depression, PTSD, and affective distress scores compared to those with mild or no neuropathic pain.[12] As such, understanding the impact of concurrent chronic pain on psychosocial outcomes may be improved by observing how these relationships differ across salient pain-related factors like interference.

To explore this relationship of TBI and chronic pain with psychosocial outcomes we utilized our work on defining extreme phenotypes, or those with best and worst outcomes, for pain interference and perceived improvement with treatment.[13,14] The purpose of the current study is to examine how psychosocial outcomes differ within extreme phenotypes defined for pain interference and perceived improvement with treatment. By examining psychosocial outcomes among individuals with chronic pain who differ phenotypically in their pain experience, our goal is to identify characteristics for potential stratification as well as modifiable targets for future interventions to improve these outcomes and to

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determine whether pain interference or perceived improvement may be more relevant in this population.

METHODS

Participants

Data from the current study were collected as part of the National Institute on Disability, Independent Living, and Rehabilitation Research Traumatic Brain Injury Model System (TBIMS) Collaborative study "The Characterization and Treatment of Chronic Pain after TBI", which is described in detail in Harrison-Felix, PhD *et al.*.[15] Briefly, TBIMS participants[16,17] were recruited from those enrolled in the TBIMS National Database (NDB) from participating centers (17 civilian and 1 VA TBIMS) at a regularly scheduled follow-up interview between May 1, 2019 and Aug 31, 2022. All centers received approval from their institutional review board. The data analyzed here include 1762 participants who reported having current chronic pain at the time of the Pain Survey.

Measures

Chronic Pain Extreme Phenotypes—*Pain interference* was measured during the Pain Survey using seven Brief Pain Inventory (BPI)[18] items that query the extent to which pain interferes with general activity, mood, walking ability, normal work, relations with other people, sleep, and enjoyment of life. Participants were asked to rank how much pain has interfered with each daily activity over the past 2 weeks on a 10-point scale from 0 (did not interfere) to 10 (completely interfered). A total pain interference score was computed as the average of these seven items.

Perceived improvement was measured during the Pain Survey using the Patient's Global Impression of Change (PGIC)[19] which asks the participant to rank their perceived change following pain treatment regarding activity limitations, symptoms, emotions, and overall quality of life on a 7-point scale (1 = no change, 2 = almost the same, 3 = a little better, 4 = somewhat better, 5 = moderately better, 6 = better, 7 = a great deal better).

Extreme phenotypes for pain interference[13] and perceived improvement,[14] were defined and are characterized in companion studies. Extreme groups were data driven and comprised of those with the best and worst outcomes defined by the tails of the distributions (upper and lower quartiles); this study utilized the same sample and cut-points as defined in these companion studies. Distributions of pain interference and perceived improvement scores are provided in Supplementary Figure 1. Participants with pain interference score ≤ 2.3 were classified into the extreme low interference phenotype and those with pain interference score ≥ 6.2 into the extreme high interference phenotype. Participants with PGIC score = 1 (no change) were classified into the extreme no change phenotype and those with PGIC score ≥ 5 (at least moderately better) into the extreme improvement phenotype. The remaining participants were classified into the non-extreme phenotype for interference and improvement each.

Psychosocial Outcomes—*Life satisfaction* was measured using the Satisfaction with Life Scale (SWLS).[20] Each of the 5 items are rated on a 7-point Likert scale (1 = strongly

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agree to 7 = strongly disagree) and items scores are summed to produce a total score (range 5-35), with higher scores indicating greater overall life satisfaction. *Post-traumatic stress symptomology* was measured using the Post-Traumatic Stress Disorder Checklist for DSM-5 (PCL-5).[21,22] Each of the 20 items are rated on a 5-point Likert scale (0 = not at all to 4 = extremely) and item scores are summed to produce a total score (range 0-80), with higher scores representing more severe PTS symptomology. *Depression symptomology* was measured using the Patient Health Questionnaire-9 (PHQ-9)[23] which assesses the frequency of the 9 DSM-IV depression criteria during the past 2 weeks. The 9 items are rated on a 4-point Likert scale (0 = not at all to 3 = nearly every day) and item scores are summed to produce a total score (range 0-27), with higher scores indicating more depression symptomology. *Anxiety symptomology* was measured using the General Anxiety Disorder-7 (GAD-7)[24] which assesses the frequency of the 7 DSM-IV anxiety criteria during the past 2 weeks. The 7 items are rated on a 4-point Likert scale (0 = not at all to 3 = nearly every day) and item scores are summed to produce a total score (range 0-21), with higher scores indicating more anxiety symptomology. *Sleep quality* was measured using the 19-item Pittsburgh Sleep Quality Index (PSQI)[25] which measures sleep quality and disturbances over a 1-month period. Seven component scores are generated which are summed to produce a total score (range 0-21), with higher scores representing poorer sleep quality. *Community participation* was measured by the 17-item Participation Assessment for Recombined Tools – Objective (PART-O) which assess participation in life roles at the societal level. Items are averaged within domains to produce domain (out and about, productivity, and social) and total (summary) scores that each range from 0-5, with higher scores indicating greater participation. All outcome measures were collected during TBIMS follow-up interview with the exception of PCL-5 and PSQI which were included in the Pain Survey.

Covariates—Covariates generally known to be associated with psychosocial outcomes were considered for adjustment in statistical analyses for all psychosocial outcome models. *Sociodemographic characteristics* included years post-injury, sex, race and ethnicity, and current (at the time of TBIMS follow-up) age, level of education, and employment status. *Functional outcome* measures included current (at the time of TBIMS follow-up) FIM™ motor and cognitive scores. Additionally, *pain intensity* was considered as an important covariate as it was the primary characteristic identified in the companion studies,[13,14] discriminating extreme phenotypes for both pain interference and perceived improvement and expected to account for additional variability in psychosocial outcomes. Pain intensity was measured during the Pain Survey using the Brief Pain Inventory (BPI)[18] and rated as 0 (no pain) to 10 (pain as bad as you can imagine) on four items: when pain is at its “worst”, “least”, “average”, and “right now”. A total pain intensity score was computed as the average of these 4 items.

Statistical Methods

All statistical analyses were conducted using SAS v.9.4 (© 2016 SAS Institute Inc., Cary, NC) assuming a 5% level of significance unless otherwise stated. Sample characteristics were summarized using means, standard deviations (SDs), and percentiles for continuous variables and frequency counts and percentages for categorical variables. Unadjusted statistical comparison of psychosocial outcomes between extreme low and high interference

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phenotypes and between extreme no change and improvement phenotypes were conducted with two-sample t-tests for normally distributed variables and Wilcoxon rank-sum tests for skewed variables.

Adjusted comparisons of psychosocial outcomes between extreme interference phenotypes and between extreme perceived improvement phenotypes were conducted using general linear models (GLM). Separate GLMs were fit for each psychosocial outcome and phenotype characteristic (interference or improvement) pair. Each GLM included an effect for extreme phenotype and effects for the covariates (follow-up period, age, sex, White race, Black race, Other race, Hispanic ethnicity, education, employment, FIM motor and cognitive scores, and pain intensity). Effect sizes (ES) were computed based on these models as the estimated difference in mean outcome between extreme phenotypes divided by the model root mean square error.[26] Effect sizes of 0.2, 0.5, and 0.8 are considered small, medium, and large, respectively. The overall percentage of variability explained by the model (R^2) with extreme phenotype (interference or improvement) and the set of covariates was estimated, as well as the R^2 explained by just the set of covariates. The differences in model R^2 (covariates plus group – covariates only) represents the percentage of variation in the outcome due to extreme phenotype.

To further understand the unique contribution of pain interference and perceived improvement above and beyond pain intensity, we assessed pain intensity as a confounding factor by comparing models with and without pain intensity (phenotype + other covariates versus phenotype + pain intensity + other covariates). Large reductions in the effect sizes for extreme phenotype when including pain intensity were noted, and suggest the relationship between extreme phenotype and psychosocial outcome is confounded by pain intensity.

GLMs were also used to explore the interaction between pain interference phenotype and perceived improvement phenotype on psychosocial outcomes. Models for each outcome included pain interference phenotypes (low, neutral, high), perceived improvement phenotypes (improvement, neutral, no change), the interaction between interference and improvement phenotypes, and the aforementioned set of covariates. As participants could be in an extreme for one phenotype (i.e., interference) and a non-extreme for the other phenotype (i.e., improvement), the neutral (non-extreme) category for both phenotypes was included in these interaction models.

RESULTS

Subject characteristics, including extreme phenotypes, covariates, and psychosocial outcome measures, are summarized for the entire sample reporting chronic pain at follow-up (N = 1762) in Table 1.

Extreme Phenotypes for Pain Interference and Perceived Improvement

Extreme phenotypes for pain interference and perceived improvement are cross-tabulated in Table 2. Only 9% of participants in the total sample were classified in the best outcome phenotype for both outcomes and 6% in the worst outcome phenotypes for both outcomes. There was also a large amount of heterogeneity of one phenotype within the levels of the

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other phenotype. For example, among those in the extreme high interference phenotype, 25% were extreme no change phenotype, 56% were non-extreme, and 19% were extreme improvement phenotype. Among those in the extreme improvement phenotype, 16% were extreme high interference phenotype, 52% were non-extreme, and 32% were the extreme low interference phenotype.

Psychosocial Outcomes across Extreme Phenotypes

The psychosocial outcomes are summarized by extreme phenotypes for both pain interference and perceived improvement in Table 3. Significantly better outcomes were observed for the extreme low versus extreme high interference phenotype and for the extreme improvement versus extreme no change phenotype. Additionally, the magnitude of the differences was larger between extreme interference phenotypes than extreme improvement phenotypes.

Covariate Adjusted Differences in Psychosocial Outcomes between Extreme Phenotypes

Pain Interference—The adjusted differences in psychosocial outcomes between extreme pain interference phenotypes after controlling for covariates are shown in Table 4. The covariates and extreme interference phenotype together accounted for 21.1%-44.4% of variability in psychosocial outcomes, with the increase in variance due to interference phenotype ranging from 0.4% to 8.8%. Across all outcomes, the extreme low interference phenotype had significantly better psychosocial outcomes than the extreme high interference phenotype. Large extreme phenotype effect sizes were observed for post-traumatic stress symptomology (ES = −1.14), sleep quality (ES = −1.10), depression (ES = −1.08), anxiety (ES = −0.82), and life satisfaction (ES = 0.76).

Pain intensity was a significant covariate for sleep quality ($p = 0.002$), but not post-traumatic stress, depression, and anxiety symptomology (p's < 0.081), nor life satisfaction or participation (p's > 0.34). When excluding pain intensity as a covariate, notably larger effect sizes were observed for post-traumatic stress, depression, and anxiety symptomology, and sleep quality (ES change > 0.1), suggesting pain intensity is an important confounding factor of the relationship between extreme interference phenotype and these outcomes.

Perceived Improvement—The adjusted differences in psychosocial outcomes between extreme perceived improvement phenotypes after controlling for covariates are shown in Table 5. The covariates and extreme improvement phenotype together accounted for 17.0%-33.0% of variability in psychosocial outcomes, with the increase in variance due to phenotype ranging from 0.0%-0.7%. While the extreme improvement phenotype had significantly better life satisfaction, overall participation, and out and about participation than the extreme no change phenotype, effect sizes were small (ES = 0.16-0.21) and less than 1% of variability was due to extreme improvement phenotype.

Pain intensity was a significant covariate for life satisfaction, post-traumatic stress, depression, and anxiety symptomology, sleep quality, overall participation, and social participation (all p's < 0.021), but not for out and about or productivity participation (p's > 0.35). When excluding pain intensity from these models, notably larger effect sizes for

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extreme improvement phenotypes were observed for post-traumatic stress, depression, and anxiety symptomology, and sleep quality (ES change > 0.1), suggesting pain intensity is also an important confounding factor of the relationships between extreme improvement phenotypes and these outcomes.

Interactions between Extreme Pain Interference and Perceived Improvement Phenotypes on Psychosocial Outcomes

As a final exploratory analysis, the interactions between pain interference phenotype and perceived improvement phenotype on psychosocial outcomes were assessed and are shown in Figure 1. The trend observed for most outcomes was that differences in psychosocial outcomes were more strongly associated with pain interference phenotyping than with perceived improvement phenotyping, after controlling for covariates. The best psychosocial outcomes were seen among the extreme low interference phenotypes and the worst psychosocial outcomes were seen among the extreme high interference phenotypes. For example, we see large differences in mean PCL-5 across the pain interference phenotypes regardless of improvement phenotyping, with the extreme high interference phenotype having the highest means and the extreme low interference phenotype having the lowest means. However, within each pain interference phenotype, small differences in mean PCL-5 are observed among the perceived improvement phenotype. For all outcomes, there was no interaction effects between pain interference and perceived improvement suggesting that the differences among improvement phenotypes are similar across the interference phenotypes (and vice versa).

DISCUSSION

This study examined differences between psychosocial factors on extreme pain phenotypes for pain interference and perceived improvement. The findings of significant differences on all psychosocial outcomes in bivariate comparisons between extreme phenotypes for both constructs support the clinical significance of these phenotypes. Although conceivably similar outcomes, our data also support that pain interference and perceived improvement are distinct constructs, with only 15.7% of individuals belonging to equivalent best or worst extreme phenotypes. This indicates perceived improvement and pain interference extreme phenotypes are unique and represent different patient characteristics and may have distinct clinical intervention needs.

In covariate adjusted analysis of pain interference extreme phenotypes, the extreme low interference phenotype continued to show significantly better outcomes on every psychosocial measure compared to the extreme high interference phenotype. Additionally, with the exception of participation (PART-O), effect sizes were large. Whereas in the adjusted models of perceived improvement, differences between the no change and improvement extremes emerged only for SWLS and Participation (Out and About and Summary Score on PART-O) with small effect sizes, and no differences were observed for other outcomes (PTS, depression, or anxiety symptomology, or sleep). Adjusted differences in psychosocial outcomes for extreme perceived improvement phenotypes also revealed

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that phenotypic group accounted for much less of the variance (0.0%-0.7%) relative to interference (0.4%-8.8%).

By including pain intensity as a covariate in all models, we were able to assess for differences in extreme phenotypes above and beyond this factor. For both constructs (pain interference, perceived improvement), pain intensity was found to be an important factor in the relationship between extreme phenotype response and psychosocial outcomes, as its inclusion resulted in a reduction in phenotype effect sizes for PTS, depression, and anxiety symptomology, and sleep quality outcomes. The combined effects of pain interference and perceived improvement were also examined in the covariate adjusted interaction models to further determine relative contribution to differences on psychosocial outcomes and findings similarly show that differences in psychosocial outcomes were more strongly associated with pain interference phenotyping than with perceived improvement phenotyping. This likely reflects a closer correspondence between the perception of improvement and the salient somatic experience of among patients, than intensity and interference.[27,28] The lesser impact of inclusion of pain intensity in the model of pain interference supports the consideration of pain interference as a differentiated outcome from pain levels when addressing psychosocial needs of those experiencing chronic pain[29] following TBI. This has important implications on clinical screening, where patients are often queried about pain solely using an intensity scale such as the 0-10 numerical rating scale[30] and on clinical evaluation where interference may also not be probed.

Expectedly then, psychosocial outcomes are significantly better for those with low pain interference than high pain interference and significantly better for those with meaningful change than no perceived change from treatment. The psychosocial factors that distinguished extreme outcomes differed across pain phenotypes (interference, improvement) which underscores the necessity for multimodal approaches to chronic pain treatment that can address a variety of psychological needs. Utilizing extreme phenotype approaches may guide research on identifying key groups of interest to determine whether interventions currently being utilized may be more or less effective in these extreme responders.

This is the first large scale study of psychosocial factors in individuals with TBI utilizing an extreme phenotype approach to understand their role in the worst and best chronic pain outcomes following injury. This was possible using a large sample size from a well-characterized and representative population of individuals who received inpatient rehabilitation following TBI 1 to 30 years previously. The study relied on self-report assessments, a mechanism to gain valuable insights into living with a condition, but carries a risk of bias due to several factors including recall, awareness, social desirability, and identity.[31] The use of ordinal outcomes in the TBIMS is a limitation and future research should consider using measures scaled to perform with interval level properties. Perceived improvement is a patient reported global outcome which lacks specificity as to what type of treatment and for what sources of pain improvement from treatment may have occurred. In addition, it may be difficult for some participants to determine whether their current experience is related to actual change (reduction in pain) vs. the general perception of feeling better in the areas noted (physical function, symptoms, emotions and overall

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function) and vice versa which may lead to inaccurately attributing improvement due to some type of pain intervention. The study does not examine the effect of specific treatments on outcomes. The cross-sectional design does not give insight to the direction of these relationships or the trajectory of pain course. Other pain and treatment characteristics not measured or included in models could explain additional variation in outcomes, or possibly confound these results.

While the TBIMS sample has been established to be largely representative of the population of adults admitted for acute, inpatient rehabilitation in the US with a primary diagnosis of TBI, the TBIMS tends to include participants with overall younger age at time of injury, higher employment rates at injury (and lower retirement rates), and longer rehabilitation length of stays.[32,33] In addition, participants who completed the Pain Survey tended to be younger at follow-up, had higher levels of education, were less likely to abstain from alcohol and more likely to be light drinkers, and tended to have better functional outcomes on the DRS and GOS-E as compared to TBIMS participants who were eligible but did not complete the pain survey, although associated effect sizes were small.[15] These differences may affect the generalizability of our results to the larger TBI population.

Further research is warranted to gain more in-depth understanding into the relationships with pain interference and treatment improvement with psychosocial function. For example, the role of specific treatments and additional personal characteristics on outcomes. Research is also needed to examine how psychosocial function after TBI impacts pain interference and perceived improvement from treatment which may also provide important insights to improve both pain and TBI care and outcomes.

CONCLUSIONS:

Pain interference and perceived improvement with treatment contribute to unique variability in psychosocial outcomes and help us better understand the complexity of living with chronic pain and TBI. We found that persons living with chronic pain following TBI who have high pain interference (versus low interference) and/or no perceived change from treatment (versus meaningful change) also had significantly poorer psychosocial function including life satisfaction, posttraumatic stress, depression, anxiety, sleep quality, and community participation. Ultimately, these results highlight the importance of routine screening of pain, pain interference, perceived improvement from treatments, and psychosocial function as part of clinical follow-up assessment and treatment of individuals living with chronic TBI.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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REFERENCES

1. Treede R-D, Rief W, Barke A, et al. Chronic pain as a symptom or a disease: the IASP Classification of Chronic Pain for the International Classification of Diseases (ICD-11). PAIN. 2019;160(1):19–27. doi:10.1097/j.pain.0000000000001384 [PubMed: 30586067]
2. Hammond FM, Corrigan JD, Ketchum JM, et al. Prevalence of Medical and Psychiatric Comorbidities Following Traumatic Brain Injury. The Journal of head trauma rehabilitation. Jul/Aug 2019;34(4):E1–e10. doi:10.1097/htr.0000000000000465
3. Portanova J, Buchanan D, Moore M, Thompson H. Factors Associated with the Development of Persistent Pain after mTBI. Pain Management Nursing. 2021/10/01/ 2021;22(5):592–598. doi:10.1016/j.pmn.2021.04.001 [PubMed: 34011466]
4. Ashina H, Al-Khazali HM, Iljazi A, et al. Psychiatric and cognitive comorbidities of persistent post-traumatic headache attributed to mild traumatic brain injury. The Journal of Headache and Pain. 2021/07/26 2021;22(1):83. doi:10.1186/s10194-021-01287-7 [PubMed: 34311696]
5. Kumar RG, Gao S, Juengst SB, Wagner AK, Fabio A. The effects of post-traumatic depression on cognition, pain, fatigue, and headache after moderate-to-severe traumatic brain injury: a thematic review. Brain Injury. 2018/03/21 2018;32(4):383–394. doi:10.1080/02699052.2018.1427888 [PubMed: 29355429]

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6. Scholten AC, Haagsma JA, Cnossen MC, Olff M, van Beeck EF, Polinder S. Prevalence of and Risk Factors for Anxiety and Depressive Disorders after Traumatic Brain Injury: A Systematic Review. Journal of Neurotrauma. 2016/11/15 2016;33(22):1969–1994. doi:10.1089/neu.2015.4252 [PubMed: 26729611]
7. Taylor BC, Hagel EM, Carlson KF, et al. Prevalence and Costs of Co-occurring Traumatic Brain Injury With and Without Psychiatric Disturbance and Pain Among Afghanistan and Iraq War Veteran VA Users. Medical Care. 2012;50(4):342–346. [PubMed: 22228249]
8. Cifu DX, Taylor BC, Carne WF, et al. Traumatic brain injury, posttraumatic stress disorder, and pain diagnoses in OIF/OEF/OND Veterans. J Rehabil Res Dev. 2013;50(9):1169–76. doi:10.1682/jrrd.2013.01.0006 [PubMed: 24458958]
9. Finan PH, Goodin BR, Smith MT. The Association of Sleep and Pain: An Update and a Path Forward. The Journal of Pain. 2013;14(12):1539–1552. doi:10.1016/j.jpain.2013.08.007 [PubMed: 24290442]
10. Kumar RG, Ketchum JM, Corrigan JD, Hammond FM, Sevigny M, Dams-O'Connor K. The Longitudinal Effects of Comorbid Health Burden on Functional Outcomes for Adults With Moderate to Severe Traumatic Brain Injury. Journal of Head Trauma Rehabilitation. 2020;35(4):E372–E381. doi:10.1097/htr.0000000000000572 [PubMed: 32108718]
11. Hanks R, Ketchum J, Peckham M, et al. Associations of Chronic Pain with Psychosocial Outcomes after Traumatic Brain Injury: A NIDILRR and VA TBI Model Systems Collaborative Project. The Journal of head trauma rehabilitation. under review.
12. Robayo LE, Govind V, Vastano R, et al. Multidimensional pain phenotypes after Traumatic Brain Injury. Front Pain Res (Lausanne). 2022;3:947562. doi:10.3389/fpain.2022.947562 [PubMed: 36061413]
13. Hoffman J, Ketchum J, Agtarap S, et al. Characterizing Extreme Phenotypes for Pain Interference in Persons with Chronic Pain following Traumatic Brain Injury: A NIDILRR and VA TBI Model Systems Collaborative Project. The Journal of head trauma rehabilitation. under review.
14. Hoffman J, Ketchum J, Agtarap S, et al. Characterizing Extreme Phenotypes for Perceived Improvement from Treatment in Persons with Chronic Pain following Traumatic Brain Injury: A NIDILRR and VA TBI Model Systems Collaborative Project. The Journal of head trauma rehabilitation. under review.
15. Harrison-Felix C, Sevigny M, Beaulieu C, et al. Characterization and Treatment of Chronic Pain after Traumatic Brain Injury -- Comparison of Characteristics between Individuals with Current Pain, Past Pain and No Pain: A NIDILRR and VA TBI Model Systems Collaborative Project. The Journal of head trauma rehabilitation. under review.
16. Dijkers MP, Harrison-Felix C, Marwitz JH. The Traumatic Brain Injury Model Systems: History and Contributions to Clinical Service and Research. The Journal of head trauma rehabilitation. 2010;25(2):81–91. doi:10.1097/HTR.0b013e3181cd3528 [PubMed: 20134334]
17. Dijkers MP, Marwitz JH, Harrison-Felix C. Thirty Years of National Institute on Disability, Independent Living, and Rehabilitation Research Traumatic Brain Injury Model Systems Center Research-An Update. The Journal of head trauma rehabilitation. Nov/Dec 2018;33(6):363–374. doi:10.1097/htr.0000000000000454 [PubMed: 30395041]
18. Cleeland CS, Ryan K. The brief pain inventory. Pain Research Group. 1991;20:143–147.
19. Hurst H, Bolton J. Assessing the clinical significance of change scores recorded on subjective outcome measures. Journal of Manipulative and Physiological Therapeutics. 2004/01/01/ 2004;27(1):26–35. doi:10.1016/j.jmpt.2003.11.003 [PubMed: 14739871]
20. Diener E, Emmons RA, Larsen RJ, Griffin S. The Satisfaction With Life Scale. Journal of personality assessment. 1985/02/01 1985;49(1):71–75. doi:10.1207/s15327752jpa4901_13 [PubMed: 16367493]
21. Blevins CA, Weathers FW, Davis MT, Witte TK, Domino JL. The Posttraumatic Stress Disorder Checklist for DSM-5 (PCL-5): Development and Initial Psychometric Evaluation. Journal of traumatic stress. 2015;28(6):489–498. doi:10.1002/jts.22059 [PubMed: 26606250]
22. Bovin MJ, Marx BP, Weathers FW, et al. Psychometric properties of the PTSD checklist for diagnostic and statistical manual of mental disorders–fifth edition (PCL-5) in veterans. Psychological assessment. 2016;28(11):1379. [PubMed: 26653052]

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23. Kroenke K, Spitzer RL, Williams JBW. The PHQ-9. Journal of General Internal Medicine. 2001;16(9):606–613. doi:10.1046/j.1525-1497.2001.016009606.x [PubMed: 11556941]
24. Spitzer RL, Kroenke K, Williams JBW, Löwe B. A Brief Measure for Assessing Generalized Anxiety Disorder: The GAD-7. Archives of Internal Medicine. 2006;166(10):1092–1097. doi:10.1001/archinte.166.10.1092 [PubMed: 16717171]
25. Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh sleep quality index: A new instrument for psychiatric practice and research. Psychiatry Research. 1989/05/01/ 1989;28(2):193–213. doi:10.1016/0165-1781(89)90047-4 [PubMed: 2748771]
26. Steiger JH. Beyond the F Test: Effect Size Confidence Intervals and Tests of Close Fit in the Analysis of Variance and Contrast Analysis. Psychological Methods. 2004;9:164–182. doi:10.1037/1082-989X.9.2.164 [PubMed: 15137887]
27. Salaffi F, Stancati A, Alberto Silvestri C, Ciapetti A, Grassi W. Minimal clinically important changes in chronic musculoskeletal pain intensity measured on a numerical rating scale. European Journal of Pain. 2004/08/01/ 2004;8(4):283–291. doi:10.1016/j.ejpain.2003.09.004 [PubMed: 15207508]
28. Ferguson L, Scheman J. Patient global impression of change scores within the context of a chronic pain rehabilitation program. The Journal of Pain. 2009;10(4):S73. doi:10.1016/j.jpain.2009.01.258
29. Wilson M Integrating the Concept of Pain Interference into Pain Management. Pain Management Nursing. 2014/06/01/ 2014;15(2):499–505. doi:10.1016/j.pmn.2011.06.004 [PubMed: 24882027]
30. Hoot MR, Khokhar B, Walker WC. Self-report Pain Scale Reliability in Veterans and Service Members With Traumatic Brain Injuries Undergoing Inpatient Rehabilitation. Military Medicine. 2019;185(3-4):370–376. doi:10.1093/milmed/usz272
31. Althubaiti A Information bias in health research: definition, pitfalls, and adjustment methods. Journal of Multidisciplinary Healthcare. 2016:211. doi:10.2147/jmdh.s104807 [PubMed: 27217764]
32. Corrigan JD, Cuthbert JP, Whiteneck GG, et al. Representativeness of the Traumatic Brain Injury Model Systems National Database. The Journal of head trauma rehabilitation. Nov-Dec 2012;27(6):391–403. doi:10.1097/HTR.0b013e3182238cdd [PubMed: 21897288]
33. Cuthbert JP, Corrigan JD, Whiteneck GG, et al. Extension of the representativeness of the Traumatic Brain Injury Model Systems National Database: 2001 to 2010. The Journal of head trauma rehabilitation. Nov-Dec 2012;27(6):E15–27. doi:10.1097/HTR.0b013e31826da983 [PubMed: 23131967]

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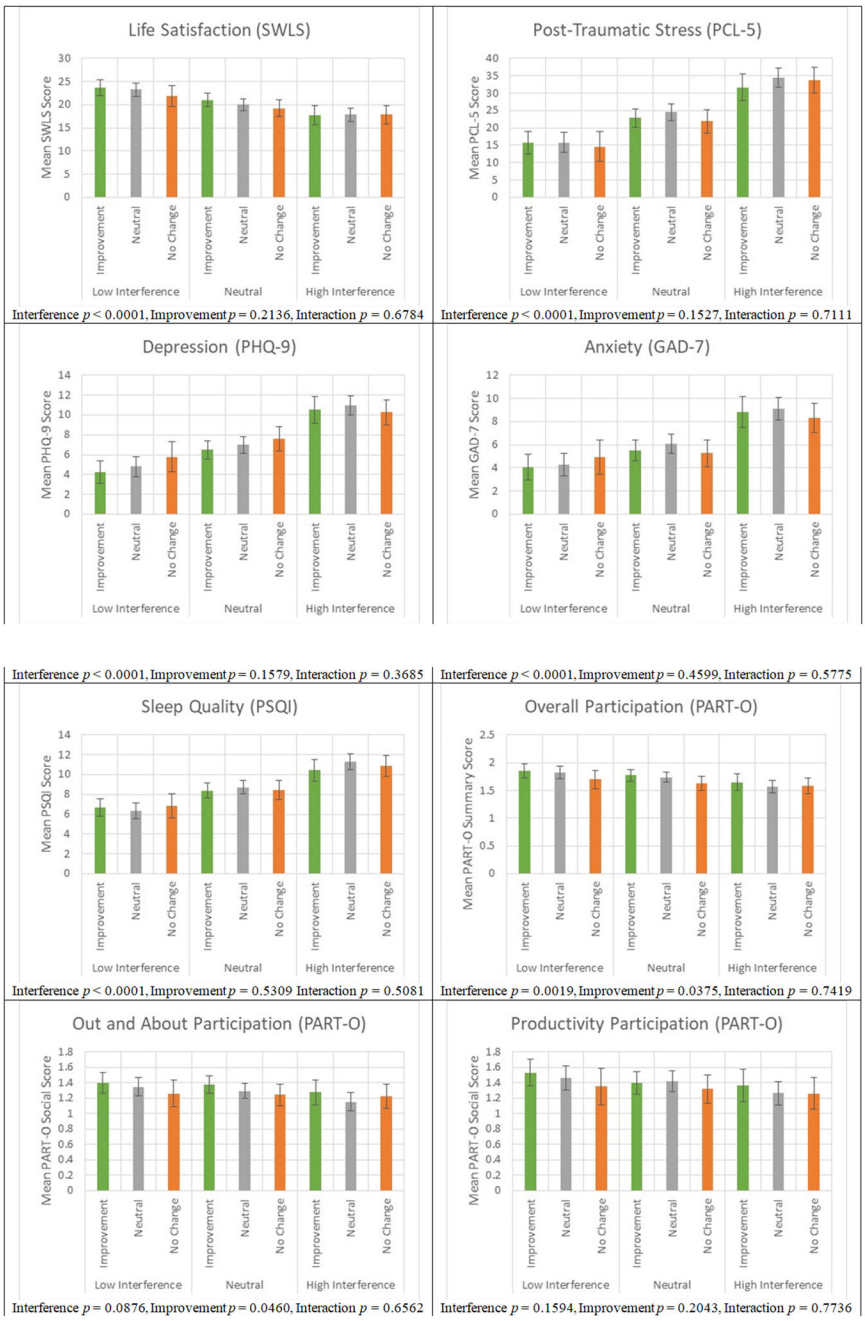

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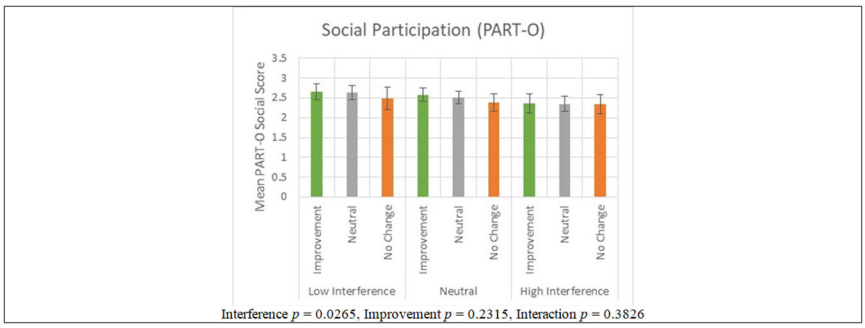

Figure 1: Interactions between Pain Interference and Perceived Improvement Phenotypes on Psychosocial Outcomes

All models adjust for follow-up period (categorical), current age, sex, white race, black race, other race, Hispanic ethnicity, current level of education, current employment status, current FIM motor cognitive scores, and current pain intensity; PART-O Productivity and Summary Models do not include employment status; SWLS = Satisfaction with Life Scale; PCL-5 = Post-Traumatic Stress Disorder Checklist for DSM-5 (PCL-5); PHQ-9 = Patient Health Questionnaire; GAD-7 = General Anxiety Disorder Questionnaire; PSQI = Pittsburgh Sleep Quality Index; PART-O = Participation Assessment with Recombined Tools – Objective

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Table 1:

Outcome Characteristics of Participants Reporting Chronic Pain

Sample Characteristics	**N = 1762**	**N [Missing]**
Chronic Pain Extreme Phenotypes		
Pain Interference Phenotypes		1727 [35]
Extreme High Interference Phenotype [BPI ≥ 6.2], N (%)	431 (25.0%)	
Non-Extreme Neutral Phenotype [2.3 < BPI < 6.2], N (%)	855 (49.5%)	
Extreme Low Interference Phenotype [BPI ≤ 2.3], N (%)	441 (25.5%)	
Perceived Improvement Phenotypes		1718 [44]
Extreme No Change Phenotype [PGIC = 1], N (%)	290 (16.9%)	
Non-Extreme Neutral Phenotype [2 ≤ PGIC ≤ 4], N (%)	916 (53.3%)	
Extreme Improvement Phenotype [PGIC ≥ 5], N (%)	512 (29.8%)	
Subject Characteristics (Covariates)		
Years Post-Injury at Follow-Up, Median (IQR)	5.4 (2.1, 14.6)	1762 [0]
1 Year, N (%)	298 (16.9%)	
2 Years, N (%)	229 (13.0%)	
5 Years, N (%)	383 (21.7%)	
10 Years, N (%)	341 (19.4%)	
15+ Years	511 (29.0%)	
Age at Follow-Up, Mean (SD)	46.4 (15.1)	1762 [1]
Sex, N Male (%)	1284 (72.9%)	1762 [0]
Race[†]		
White, N (%)	1322 (75.3%)	1756 [6]
Black / African American Only, N (%)	329 (18.7%)	1757 [5]
Other, N (%)	119 (6.8%)	1756 [6]
Hispanic, Latino, or Spanish Ethnicity, N (%)	209 (11.9%)	1759 [3]
Education Level at Follow-Up		1757 [5]
Less than High School, N (%)	285 (16.2%)	
High School (including Other), N (%)	422 (24.0%)	
Some College / Associate's Degree, N (%)	654 (37.2%)	
Bachelor's Degree or Higher, N (%)	396 (22.5%)	
Employment Status at Follow-Up		1756 [6]
Employed/Student, N (%)	687 (39.1%)	
Retired, N (%)	719 (40.9%)	
Unemployed, N (%)	258 (14.7%)	
Other, N (%)	92 (5.2%)	
FIM Motor at Follow-Up, Median (IQR)	88 (83, 91)	1741 [21]
FIM Cognitive at Follow-Up, Median (IQR)	32 (29, 34)	1739 [23]
Pain Intensity (BPI), Mean (SD)	4.7 (1.9)	1741 [21]
Psychosocial Outcomes		

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Sample Characteristics	N = 1762	N [Missing]
SWLS (Life Satisfaction), Mean (SD)	20.4 (8.2)	1541 [221]
PCL-5 (PTSD Symptoms), Median (IQR)	19 (8, 34)	1684 [78]
PHQ-9 (Depression Symptoms), Median (IQR)	7 (3, 12)	1667 [95]
GAD-7 (Anxiety Symptoms), Median (IQR)	5 (2, 10)	1671 [91]
PSQI (Sleep), Median (IQR)	8 (5, 12)	1670 [92]
PART-O Summary (Participation), Mean (SD)	1.8 (0.7)	1753 [9]
PART-O Out and About (Participation), Mean (SD)	1.4 (0.7)	1753 [9]
PART-O Productivity (Participation), Mean (SD)	1.5 (1.0)	1756 [6]
PART-O Social (Participation), Mean (SD)	2.5 (1.0)	1754 [8]

SD = standard deviation; IQR = interquartile range; BPI = Brief Pain Inventory; PGIC = Patient's Global Impression of Change; † Participants may self-report more than one race and Other includes Asian, American Indian or Alaskan Native, Native Hawaiian or Pacific Islander); SWLS = Satisfaction with Life Scale; PCL-5 = Post-Traumatic Stress Disorder Checklist for DSM-5 (PCL-5); PHQ-9 = Patient Health Questionnaire; GAD-7 = General Anxiety Disorder Questionnaire; PSQI = Pittsburgh Sleep Quality Index; PART-O = Participation Assessment with Recombined Tools – Objective

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Table 2:

Extreme Chronic Pain Phenotypes: Pain Interference by Perceived Improvement

(row % / col %)	Perceived Improvement Phenotype			
Pain Interference Phenotype	**No Change**	**Neutral**	**Improvement**	**Total**
High Interference	107 (25.3% / 37.2%)	235 (55.6% / 25.8%)	81 (19.1% / 16.0%)	423
Neutral	117 (13.9% / 40.6%)	462 (54.8% / 50.7%)	264 (31.3% / 52.2%)	843
Low Interference	64 (14.6% / 22.2%)	215 (49.0% / 23.6%)	160 (36.4% / 31.7%)	439
Total	288	912	288	1705

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Table 3:

Psychosocial Outcomes by Extreme Pain Interference and Perceived Improvement Phenotypes

	Extreme Pain Interference Phenotype			Extreme Perceived Improvement Phenotype		
Psychosocial Outcomes[§]	**Low Interference N = 441**	**High Interference N = 431**	***p*-value**	**Improvement N = 512**	**No Change N = 290**	***p*-value**
SWLS (Life Satisfaction), Mean (SD)	24.5 (7.3)	16.4 (8.3)	**< 0.0001**[a]	21.9 (7.8)	18.5 (8.4)	**< 0.0001**[a]
PCL-5 (PTSD Symptoms), Median (IQR)	9 (3, 18.5)	35 (19, 50)	**< 0.0001**[b]	16.5 (7, 30)	19 (8, 37)	**0.0278**[b]
PHQ-9 (Depression Symptoms), Median (IQR)	3 (1, 7)	12 (7, 17)	**< 0.0001**[b]	5 (2, 10)	8 (3, 14)	**< 0.0001**[b]
GAD-7 (Anxiety Symptoms), Median (IQR)	2 (0, 6)	10 (5, 15)	**< 0.0001**[b]	4 (1, 8)	6 (2, 11)	**0.0096**[b]
PSQI (Sleep), Median (IQR)	5 (3, 8)	12 (8, 15)	**< 0.0001**[b]	7 (4, 11)	9 (5, 13)	**0.0012**[b]
PART-O Summary (Participation), Mean (SD)	2.01 (0.65)	1.45 (0.67)	**< 0.0001**[a]	1.92 (0.67)	1.58 (0.70)	**< 0.0001**[a]
PART-O Out and About (Participation), Mean (SD)	1.54 (0.66)	1.11 (0.68)	**< 0.0001**[a]	1.50 (0.67)	1.23 (0.68)	**< 0.0001**[a]
PART-O Productivity (Participation), Mean (SD)	1.72 (0.98)	1.11 (0.89)	**< 0.0001**[a]	1.62 (0.99)	1.24 (0.93)	**< 0.0001**[a]
PART-O Social (Participation), Mean (SD)	2.76 (0.98)	2.14 (1.05)	**< 0.0001**[a]	2.65 (0.99)	2.25 (1.06)	**< 0.0001**[a]

SD = standard deviation; IQR = interquartile range; a: two-sample test; b: Wilcoxon rank-sum test; SWLS = Satisfaction with Life Scale; PCL-5 = Post-Traumatic Stress Disorder Checklist for DSM-5 (PCL-5); PHQ-9 = Patient Health Questionnaire; GAD-7 = General Anxiety Disorder Questionnaire; PSQI = Pittsburgh Sleep Quality Index; PART-O = Participation Assessment with Recombined Tools – Objective; a: two-sample t-test; b: Wilcoxon rank-sum test; c: chi-square test

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Table 4:

Differences in Extreme Pain Interference Phenotypes Adjusted for Covariates

Outcome	Difference† (SE)	Phenotype *p*-value	Covariates + Phenotype Model R^2	R^2 Increase for Phenotype	Effect Size for Phenotype
SWLS (Life Satisfaction)	5.70 (0.83)	**< 0.0001**	28.4%	4.6%	0.76
PCL-5 (PTSD Symptoms)	−17.02 (1.55)	**< 0.0001**	44.4%	8.4%	−1.14
PHQ-9 (Depression Symptoms)	−5.59 (0.54)	**< 0.0001**	43.7%	7.6%	−1.08
GAD-7 (Anxiety Symptoms)	−4.20 (0.54)	**< 0.0001**	35.4%	5.0%	−0.82
PSQI (Sleep)	−4.35 (0.41)	**< 0.0001**	37.2%	8.8%	−1.10
PART-O Summary (Participation)	0.21 (0.06)	**0.0004**	36.9%	0.9%	0.36
PART-O Out and About (Participation)	0.13 (0.06)	**0.0386**	24.6%	0.4%	0.21
PART-O Productivity (Participation)	0.21 (0.08)	**0.0130**	33.9%	0.5%	0.25
PART-O Social (Participation)	0.21 (0.10)	**0.0306**	21.1%	0.4%	0.22

All models adjust for follow-up period (categorical), current age, sex, White race, Black race, Other race, Hispanic ethnicity, current level of education, current employment status, current FIM motor cognitive scores, and current pain intensity; PART-O Productivity and Summary Models do not include employment status; † Difference computed as low – high interference; SE = standard error; R^2 Increase represents the increase in R^2 when Group is added to the covariate model; Effect size is computed as the mean difference (positive – negative) divided by the model root mean square error; SWLS = Satisfaction with Life Scale; PCL-5 = Post-Traumatic Stress Disorder Checklist for DSM-5 (PCL-5); PHQ-9 = Patient Health Questionnaire; GAD-7 = General Anxiety Disorder Questionnaire; PSQI = Pittsburgh Sleep Quality Index; PART-O = Participation Assessment with Recombined Tools – Objective

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Table 5:

Differences in Extreme Perceived Improvement Phenotypes Adjusted for Covariates

Outcome	Difference† (SE)	Phenotype *p*-value	Covariates + Phenotype Model R^2	R^2 Increase for Phenotype	Effect Size for Phenotype
SWLS (Life Satisfaction)	1.52 (0.65)	**0.0198**	17.0%	0.7%	0.20
PCL-5 (PTSD Symptoms)	0.29 (1.24)	0.8136	27.8%	<0.1%	0.02
PHQ-9 (Depression Symptoms)	−0.83 (0.45)	0.0630	27.1%	0.3%	−0.15
GAD-7 (Anxiety Symptoms)	0.00 (0.41)	0.9952	24.5%	<0.1%	<0.01
PSQI (Sleep)	−0.18 (0.35)	0.6193	17.7%	<0.1%	−0.04
PART-O Summary (Participation)	0.12 (0.05)	**0.0114**	31.2%	0.6%	0.21
PART-O Out and About (Participation)	0.10 (0.05)	**0.0463**	20.9%	0.4%	0.16
PART-O Productivity (Participation)	0.11 (0.07)	0.0887	33.0%	0.3%	0.14
PART-O Social (Participation)	0.13 (0.08)	0.0828	17.1%	0.3%	0.14

All models adjust for follow-up period (categorical), current age, sex, white race, black race, other race, Hispanic ethnicity, current level of education, current employment status, current FIM motor cognitive scores, and current pain intensity; PART-O Productivity and Summary Models do not include employment status; † Difference computed as improvement – no change; SE = standard error; R^2 Increase represents the increase in R^2 when Group is added to the covariate model; Effect size is computed as the mean difference (positive – negative) divided by the model root mean square error; SWLS = Satisfaction with Life Scale; PCL-5 = Post-Traumatic Stress Disorder Checklist for DSM-5 (PCL-5); PHQ-9 = Patient Health Questionnaire; GAD-7 = General Anxiety Disorder Questionnaire; PSQI = Pittsburgh Sleep Quality Index; PART-O = Participation Assessment with Recombined Tools – Objective