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ORIGINAL ARTICLE CLINICAL STUDIES

Predictors and Functional Outcomes Associated With Longitudinal Trajectories of Anxiety and Depression from 2 to ≥36 Months After Moderate to Severe Traumatic Brain Injury

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Abstract

This study investigated longitudinal trajectories of anxiety and depressive symptoms following moderate-severe traumatic brain injury (TBI), predictors of the trajectories, and associations with 1-year return to productivity. One hundred forty-eight patients with moderate-severe TBI were assessed at 2, 5, 12, and ≥36 months post-injury on the Beck Anxiety Inventory and the Beck Depression Inventory. Clinical interviews obtained information about demographics, injury characteristics, and 1-year return to productivity. Latent growth mixture modeling identified trajectories of anxiety and depression across time. The three-step method identified predictors of trajectories, and χ^2 analyses determined associations between trajectories and 1-year return to productivity. Analyses revealed that four-class models of anxiety and depression best fit the data. Most individuals had stable minimal (67%) or low (18%) levels of anxiety over time. Two other subsets of individuals were classified by anxiety that worsened rapidly (7%) or improved in the 1st year but worsened by 3 years post-injury (9%). Similarly for the depression trajectories, most individuals had stable minimal (70%) or low (10%) levels of depression over time. Others had depression that worsened rapidly (12%) or was delayed, with onset 1-year post-injury (8%). Predictors of worsening anxiety and depression included younger age, less education, and male gender. Those with worsening anxiety or depression were less likely to return to productivity by 1-year post-injury. There is a significant burden of anxiety (15%) and depression (20%) in the 3 years after moderate-severe TBI. Future research targeting at-risk patients may help to improve quality of life and functional recovery.

Keywords: anxiety; depression; rehabilitation; traumatic brain injury

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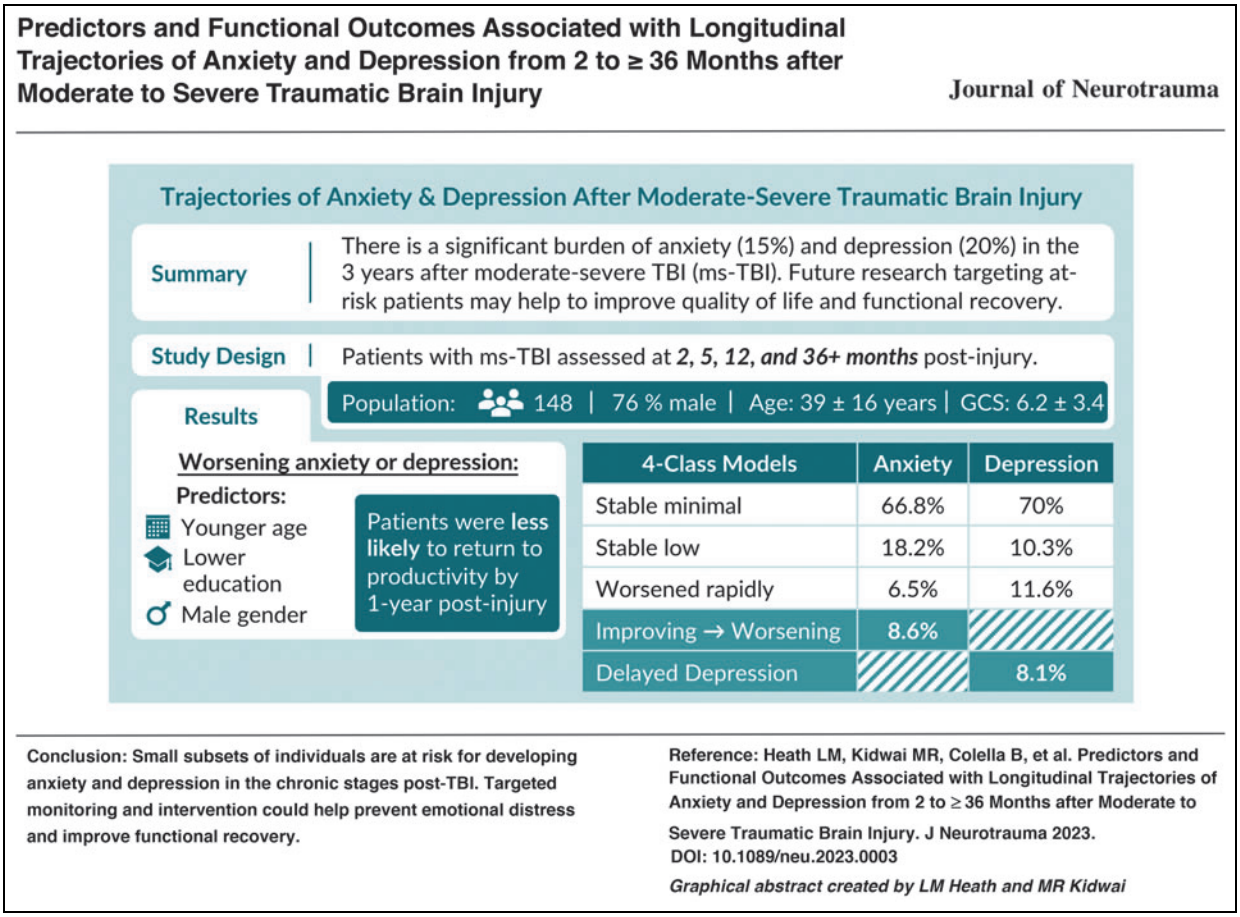

Introduction

One of the most disabling consequences of moderate-severe traumatic brain injury (TBI) is psychiatric disturbance.[1,2] Anxiety and depression are particularly prevalent;[3,4] observed in up to 50% of individuals in the acute, sub-acute, and chronic stages;[5–8] and associated with exacerbated cognitive impairments, reduced return to productivity,[9] poorer life satisfaction,[10,11] and elevated suicidality.[12]

Our understanding of how anxiety and depression prevalence and severity unfold over time is limited, and this impedes prognostication and management. Longitudinal studies have typically utilized *mean* scores, which assume a *homogeneous* pattern of change over time. A more granular approach, trajectory analysis, allows for variation in how individuals change over time and can reveal trajectory subgroups. Further, latent growth mixture models (LGMMs) permit variability of growth parameters (e.g., intercept and slope) within trajectory subgroups. Although they are more computationally demanding and requiring larger samples, LGMMs more likely reflect reality than other statistical methodology.[13] To date, only one moderate-severe TBI study has explored anxiety with trajectory analysis. In 129 adults with severe TBI measured at 3, 6, 12, and 24 months post-injury[14] two trajectories emerged: one subgroup with stable, low anxiety (69%) and the other with stable, high anxiety (31%). Only three studies, including the one referenced, have examined depression trajectories. In all three, most individuals showed stable, low levels of depression. But there were additional subgroups for whom depression was consistently high or worsening over time.[14–16] People with growing anxiety and depression are of particular interest clinically, as these individuals may be discharged from TBI treatment with intact moods and decline later when they are no longer receiving treatment.

Understanding the predictors of trajectory subtypes could further enhance management and prognostication. To date, no demographic or injury severity factors were found to be predictive of low-stable or high-stable anxiety.[14] Worsening depression trajectories were predicted by greater injury severity. Among demographic predictors, findings have been mixed for the association of age, gender, and education on depression trajectory subgroup membership, requiring further elucidation.[14–16] Additionally, two of the three trajectory studies did not exclusively examine *moderate-severe* TBI, which is important given the significant neuropathological and psychosocial differences between mild TBI/concussion and moderate-severe TBI.[17,18]

Given these gaps in the literature, the present study examined patients at approximately 2, 5, 12, and ≥36 months following moderate-severe TBI, and measured trajectories of anxiety and depression, and demographic and injury-related predictors of trajectories. We also examined associations between trajectory sub-types and 1-year return to productivity, which has yet to be examined. We hypothesized that most individuals would fit into stable low anxiety and depression groups, with smaller subgroups showing stable high or increasing anxiety and depression. We also hypothesized that worsening anxiety and depression would be associated with lower return to productivity.

Methods

Participants and procedures

Participant data (Table 1) were drawn from a larger, prospective, longitudinal study (the Toronto TBI Recovery Study). Parent study enrollment took place from 2001 to 2014 from the neurorehabilitation program of a large, urban, Canadian rehabilitation hospital. Behavioral assessments were conducted at ~2, 5, 12, and ≥36 months following moderate-severe TBI. Patients were eligible for study inclusion if they met the following criteria: (1) moderate-severe TBI as indexed by a Glasgow Coma Scale[19] score of ≤12 and/or post-traumatic amnesia (PTA) lasting ≥24 h, (2) resolution of PTA by 3 months post-injury, (3) age 18–80 years, (4) functional command of English, and (5) competency to provide informed consent for the study or availability of a legal decision maker. Exclusion criteria included: (1) prior history of TBI or stroke, (2) history of psychotic disorder, and (3) failure on a test of symptom validity (Test of Memory Malingering)[20] at any of the assessments. See Green and coworkers[21] for full details of the parent study. Current study participants additionally required: completion of the Beck Anxiety Inventory (BAI)[22] and the Beck Depression Inventory (BDI)[23] for at least two of the four time points, and no strokes or additional TBIs after the index injury. Demographic and injury characteristics (Table 1) were obtained through review of medical records and the clinical interview, which at 1-year post-injury obtained information about whether individuals had returned to their previous roles. This included paid employment (full or part time), volunteer employment, school, parenting, home-making, and active retirement. Information on pre-morbid and current activities was corroborated by caregivers where possible. Two trained clinicians reached consensus to dichotomize this information to ascertain return to productivity.[24] The study protocol was approved by the Research Ethics Board at the Toronto Rehabilitation Institute, where the study was conducted. The procedures of the study were in accordance with the standards of the Research Ethics Board.

Table 1. Summary of Sample Characteristics ($n = 148$)

Sex (% male)	76% (113)
Age at injury	38.7 ± 16.36
Years of education	13.56 ± 3.04
Race	
White	78% (115)
Asian	12% (17)
Black	5% (7)
Other	6% (9)
Lowest GCS, $n = 129$	6.22 ± 3.42
Length of PTA, $n = 126$	
< 5 min	1% (1)
1-24 h	1% (1)
1-7 days	21% (26)
1-4 weeks	56% (71)
> 4 weeks	21% (27)
Type of injury, $n = 146$	
Motor vehicle accident	60% (88)
Fall	32% (46)
Assault	6% (8)
Sports-related	3% (4)
Psychiatric history, $n = 138$	20% (28)

Values are presented as % (n) or mean ± SD.

GCS, Glasgow Coma Scale Score; PTA, post-traumatic amnesia; SD, standard deviation.

Materials

The BAI and BDI are 21-item self-report measures of anxiety and depression symptoms, respectively, with divergent validity, strong test-retest reliability,[25] and internal consistency for the TBI population.[26] Recommended cutoff scores of 0–7 for minimal anxiety, 8–15 for mild anxiety, 16–25 for moderate anxiety, and 26–63 for severe anxiety were employed for the BAI.[26] For depression, most participants were assessed using the BDI-IA.[27] Those with BDI-II scores, which are highly correlated to the BDI-IA, were converted to the BDI-IA using a conversion score .[28] Recommended cutoff scores of 0–9 for minimal depression, 10–18 for mild depression, 19–29 for moderate depression, and 30–63 for severe depression were employed for the BDI.[27]

Statistical analyses

Repeated measures analysis of variance (ANOVA) with BAI and BDI scores over time were performed to demonstrate the difference in results when the sample was collapsed across a homogeneous group mean. Growth models were conducted using *Mplus* version 7.4[29] and employed robust maximum likelihood estimation. Full information maximum likelihood (FIML) was applied to address missing data, which were assumed to be missing at random.

Separate models were run for trajectories of anxiety (BAI) and depression (BDI) across the four time points. See supplementary text for results of a single latent class growth analysis comparing linear to non-linear models. Unconditional LGMMs were compared to test two-, three-, four-, and five-class solutions with intercept,

slope, and quadratic growth parameters. Initially, the variances of all growth factors were freely estimated within classes. When models failed to converge, constraints to the within-class growth factor variances were applied, informed by TECH4 output of the covariance matrices. All other *Mplus* default specifications were retained. See supplementary text for further information about model constraints.

Optimal number of latent classes was determined by lower Bayesian Information Criterion (BIC) value, bootstrap likelihood ratio test (BLRT) p values lower than $p = 0.05$, and entropy value close to 1.00 but at least 0.80. Once the model with the optimal number of classes was identified, the three-step method with adjustment for classification errors was used to assess predictors of class membership through multinomial regression analyses.[30] Chi-Square tests examined associations between anxiety and depression trajectories, and between trajectory class memberships and 1-year return to previous roles.

Results

Participants

There were no significant differences, and small effect sizes, in demographic factors of age, sex, race, years of education, TBI severity, psychiatric history, or type of injury, between those included in the models ($n = 148$) and those excluded because of missing data ($n = 35$). Demographic and injury characteristics for the participants included in the study are presented in Table 1.

Repeated measures ANOVA

Anxiety. Repeated measures ANOVA of BAI scores violated Mauchly's test of sphericity, χ^2 (5) = 17.67, $p = 0.003$, $\varepsilon = 0.84$; therefore, Huynh–Feldt corrected results are reported. There was no significant effect of time on BAI scores, $F(2.62, 165.09) = 1.32$, $p = 0.27$. Mean ± standard deviation (SD) BAI scores were 5.17 ± 4.18, 5.67 ± 6.05, 5.73 ± 5.59, and 6.63 ± 7.33 at T1-T4, respectively.

Depression. Mauchly's test indicated a violation of the sphericity assumption, χ^2 (5) = 36.71, $p = 0.0001$, $\varepsilon = 0.75$; therefore, Huynh–Feldt corrected results are reported. There was no significant effect of time on BDI scores, $F(2.35, 117.55) = 2.59$, $p = 0.07$. Mean ± SD BDI scores were 7.96 ± 5.16, 9.18 ± 6.31, 9.8 ± 8.87, and 10.92 ± 9.48 at T1-T4, respectively.

Trajectory analysis

Anxiety. Table 2 provides the fit indices for unconditional one- to five-class growth mixture models of anxiety. Overall, best fit indices supported the four-class model. Although the five-class model had the lowest BIC, other indices suggested poorer fit, including lower entropy, lower probabilities (< 0.85) that individuals were correctly placed into their classes, and lack of clinically meaningful interpretation of a fifth class. Table 3 provides the parameter estimates of the growth factors for the classes in the four-class model.

Table 2. Fit Indices for Unconditional 1- to 5-Class Growth Mixture Models of Anxiety and Depression ($n = 148$)

	Anxiety			*Depression*		
	BIC	*BLRT*	*Entropy*	*BIC*	*BLRT*	*Entropy*
1-class	3011.234	–	–	3058.50	–	–
2-classes	2967.849	0.00001	0.882	3007.268	0.00001	0.68
3-classes	2956.928	0.00001	0.917	2996.885	0.00001	0.779
4-classes	2952.472	0.00001	0.808	2993.902	0.00001	0.816
5-classes	2943.827	0.00001	0.741	3017.335	0.1923	0.772

BIC, Bayesian information criteria; BLRT, Parametric Bootstrapped Likelihood Ratio Test.

Anxiety trajectory interpretation. Figure 1 depicts the anxiety class trajectories. Approximately 67% of individuals were classified into a stable, minimal anxiety class. This group had a mean initial BAI score of ~4, which remained relatively stable with a non-significant slope over time. A second class of individuals (18%) fit into a stable, low anxiety class, with a starting BAI score of ~9 and no significant growth over time. The other two classes showed worsening of anxiety symptoms over time, reaching moderate-severe levels by the fourth time point but following different patterns of growth. The ''rapidly worsening anxiety'' class (7%) had low symptoms at T1 (mean BAI = 6) that steeply increased in the 1st year (mean BAI = 19) and continued to increase by T4 (mean BAI = 26). The ''improving to worsening'' class (9%) had moderate symptoms at T1 (mean BAI = 16), which improved by T2 (mean BAI = 10), and improved further by T3 (mean BAI = 5), but worsened from 12 to ≥36 months post-injury (mean BAI = 25).

Depression. Two- to five-class unconditional LGMMs were tested to determine the optimal number of classes for depression over time. Model fit indices found the four-class model to best fit the data, as shown in Table 2. Additionally, the model demonstrated high probabilities of individuals being correctly classified into the four classes. Table 4 shows the parameter estimates of the growth factors for the four-class model.

Depression trajectory interpretation. Figure 2 depicts the depression class trajectories. Most individuals (70%) were classified into a stable, minimal depression class (mean BDI = 6), with no significant slope. A second class of individuals (10%) were in a stable, low level of depression class (mean BDI = 19, 16 at T1 and T4). The linear

Table 3. Mean Scores for the Growth Factors of the Four-Class Growth Mixture Model of Anxiety ($n = 148$)

	Class 1 (Stable minimal)		*Class 2 (Stable low)*		*Class 3 (Rapid worsening)*		*Class 4 (Early improving, chronically worsening)*	
Growth factors	*Mean*	*SE*	*Mean*	*SE*	*Mean*	*SE*	*Mean*	*SE*
Intercept	3.98***	0.42	8.21***	1.70	6.31**	1.84	14.54***	1.69
Linear	-1.20	0.87	4.50	2.38	19.43***	4.78	-15.05***	2.16
Quadratic	0.30	0.24	-1.27	0.67	-3.84**	1.24	5.43***	0.62

**$p < 0.01$, ***$p < 0.001$.
SE, standard error.

and quadratic growth factors were not significant, indicating that BDI scores were relatively stable across time. The other two classes showed worsening of depressive symptoms over time with different patterns of growth. The ''rapidly worsening depression'' class (8%) had a low level of symptoms at T1 (mean BDI = 9) that increased at T2, T3, and T4 (mean BDI = 16, 23, 26, respectively). The ''delayed depression'' class (12%) had minimal symptoms in the first 12 months post-injury (BDI = 7), but symptoms significantly increased at T4 (mean BDI = 29).

Associations between anxiety and depression trajectory groups

The four classes of anxiety trajectory were dichotomized into two groups: the stable minimal-low trajectories were collapsed together and the rapid worsening and early improving to chronically worsening anxiety trajectories were collapsed together. Similarly, the four depression trajectory classes were collapsed into a stable, minimal-low group and a worsening (rapid or delayed) depression group. There was a significant pairwise association between trajectory group membership for anxiety and depression (χ^2 [1, $n = 148$] = 22.56, $p < 0.001$, Cramer's V = 0.39). Most individuals with stable, minimal-low anxiety were also in the stable, minimal-low depression group (92%). Approximately half (46%) of individuals with worsening anxiety also had worsening depression.

Predictors of trajectory class membership

Anxiety. Table 5 displays the results of the multinomial logistical regression analyses for predictors of the anxiety trajectory classes. Using the stable, minimal anxiety class as the reference group, the rapidly worsening group was significantly younger. There were no other significant differences between any of the groups on factors of sex, age, years of education, TBI severity, or psychiatric history

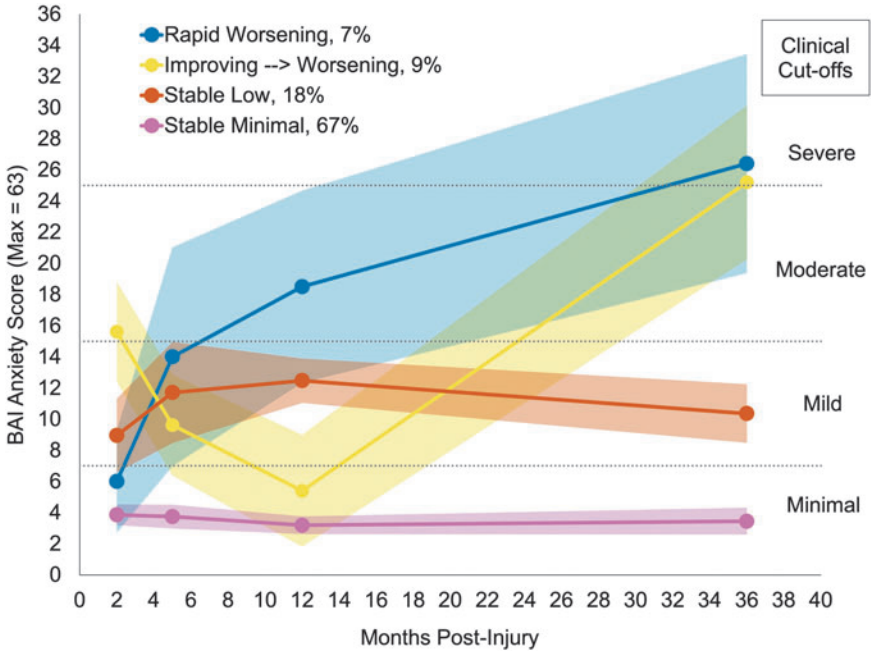

FIG. 1. Trajectories of anxiety symptoms from 2 to ≥36 months after moderate to severe traumatic brain injury (TBI) ($n = 148$). Shaded areas represent 95% confidence intervals.

Table 4. Mean Scores for the Growth Factors of the Four-Class Growth Mixture Model of Depression ($n = 148$)

	Class 1 (Stable minimal)		*Class 2 (Stable low)*		*Class 3 (Rapid worsening)*		*Class 4 (Delayed depression)*	
Growth factors	*Mean*	*SE*	*Mean*	*SE*	*Mean*	*SE*	*Mean*	*SE*
Intercept	5.89***	0.42	20.11***	2.76	9.14***	1.74	6.75***	1.43
Linear	-0.25	0.19	-4.85	4.03	21.02***	4.57	-1.49	3.93
Quadratic	–	–	1.03	0.98	-4.78***	1.6	2.35*	1.06

*$p < 0.05$, ***$p < 0.001$.
SE, standard error.

Depression. Table 6 displays the results of the multinomial logistical regression analyses for predictors of the depression trajectory classes, using the stable, minimal class as the reference group. The delayed depression group was more likely to be male and significantly younger than any of the other groups. Additionally, the rapidly worsening depression group had significantly fewer years of education than the stable, minimal group.

Relationship with return to productivity

Return to productivity at 1-year post-injury was associated with anxiety class trajectory. Those with stable, minimal-low anxiety were more likely to return to productivity (34%) than those with worsening anxiety (5%), χ^2 (1, $n = 126$) = 6.27, $p = 0.012$, Cramer's V = 0.22. Return to productivity at 1 year post-injury did not significantly differ between those with stable minimal-low depression (32%) and those with worsening depression (11%), χ^2 (1, $n = 126$) = 3.37, $p = 0.066$, Cramer's V = 0.16. When analyzing the four depression classes separately, there was a significant difference between groups (χ^2 [3, $n = 126$] = 8.59, $p = 0.035$, Cramer's V = 0.26), such that 20% of the delayed depression group had returned to previous roles at 1 year post-injury compared with 8% of the rapidly worsening depression group. However, findings should be interpreted with caution because of low cell sizes within classes.

Discussion

The current study identified four clinically meaningful trajectories of growth for both anxiety and depression across 2, 5, 12, and ≥36 months (T1–T4) after moderate-severe TBI. Although many individuals had minimal or low levels of anxiety or depression that were stable over time, there were distinct groups of individuals for whom emotional distress changed over time, with

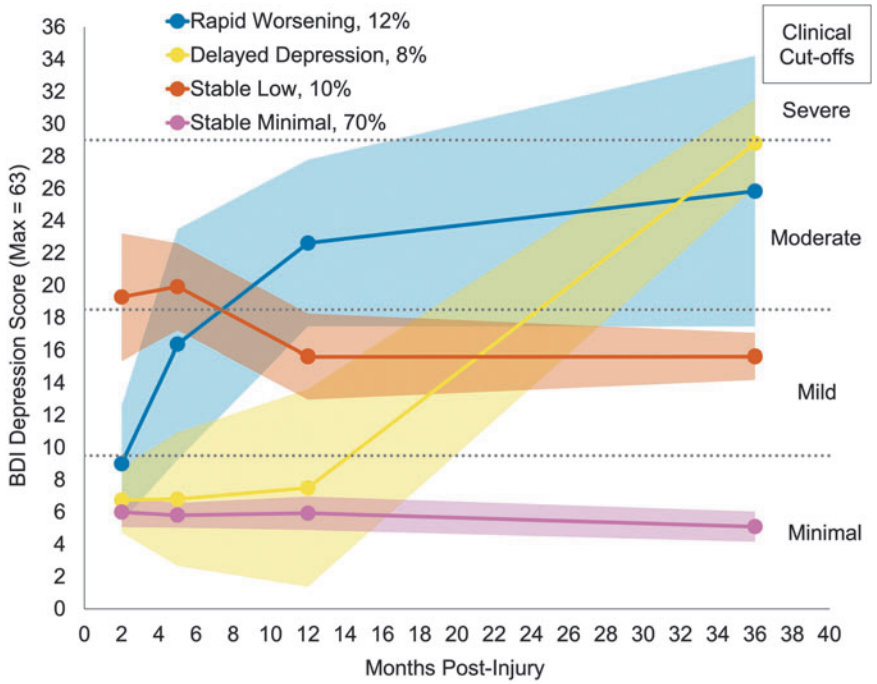

FIG. 2. Trajectories of depression symptoms from 2 to ≥36 months after moderate to severe traumatic brain injury (TBI) ($n = 148$). Shaded areas represent 95% confidence intervals .

Table 5. Multinomial Logistical Regression for Predictors of Anxiety Class Membership

	Class 1 (Stable minimal[a])		*Class 2 (Stable low)*		*Class 3 (Rapid worsening)*		*Class 4 (Improve → worsening)*	
Variables	*Est (SE)*	*Mean (SD)*	*Est (SE)*	*Mean (SD)*	*Est (SE)*	*Mean (SD)*	*Est (SE)*	*Mean (SD)*
Sex[b]	–	1.21 (0.41)	-0.46 (0.9)	1.15 (0.37)	0.62 (0.96)	1.33 (0.5)	1.4 (0.81)	1.46 (0.52)
Age	–	39.85 (17.2)	0.001 (0.02)	41.35 (14.23)	**-0.05 (0.03)***	**28.78 (11.29)**	-0.03 (0.02)	32.08 (11.79)
Years of education	–	13.50 (3.14)	0.09 (0.1)	14.5 (2.59)	-0.21 (0.13)	12.44 (2.13)	-0.01 (0.16)	13.38 (3.38)
TBI severity[c]	–	-0.02 (0.78)	-0.13 (0.38)	-0.07 (0.68)	-0.01 (0.71)	0.03 (0.88)	0.39 (0.47)	0.15 (0.7)
Psychiatric history[d]	–	0.17 (0.38)	0.54 (0.85)	0.26 (0.45)	1.16 (0.88)	0.33 (0.5)	0.77 (0.84)	0.25 (0.45)

Boldface represents statistically significant predictor.
[a]Stable minimal class served as the referent.
[b]Male = 1 and female = 2.
[c]TBI severity measured as an aggregate z-score of GCS, PTA, and length of acute care stay.
[d]0 = no and 1 = yes.
*$p < 0.05$.
Est, estimate; SE, standard error; SD, standard deviation; TBI, traumatic brain injury; GCS, Glasgow Coma Scale; PTA, post-traumatic amnesia.

varying patterns of growth. Of particular concern are those patients who initially experienced low levels of depression and anxiety, but who – likely long after discharge from inpatient or outpatient care – showed significant increases in the chronic stages of injury. These findings contrast with the results of standard, repeated measures methodology, which did not find any significant differences in anxiety or depression scores across time, highlighting the importance of employing sophisticated modeling strategies that do not assume all individuals follow the same homogeneous pattern of growth.

Anxiety trajectories

In the anxiety trajectory analysis of 148 individuals, 67% had stable BAI scores in the minimal range across time. Another 18% had anxiety scores in the mild range that did not significantly change over time. The remaining 15% of the sample were divided into two different trajectories of growth that reported anxiety in the moderate to severe range by ≥36 months post-injury. In a rapidly worsening anxiety group, individuals had an average BAI score in the minimal range at 2 months post-injury, which rapidly worsened across each time point (BAI = 6, 14, 19, and 26 at T1–T4, respectively). A second group of individuals reported anxiety in the moderate range at 2 months post-injury, which steadily improved over the 1st year post-injury (BAI = 16, 10, 5 at T1, T2, T3, respectively). However, by ≥36 months post-injury, anxiety among these individuals notably increased to a mean BAI of 25, suggesting a pattern of early improvement in the 1st year after TBI, which relapsed beyond previous levels to reach moderate-severe anxiety by 3 years post-injury.

Although anxiety trajectories have only been modeled in one previous study to the best of our knowledge,[14] our results of a majority of individuals reporting low stable anxiety are consistent with previous findings. However, Ren and coworkers[14] reported one other class, consisting of individuals reporting high stable anxiety, and our study found two distinct classes of worsening anxiety. Clinically, it has been shown that anxiety can follow nonlinear trajectories over time, improving and worsening over a span of years.[31] Some individuals may have a steady worsening of anxiety as they adjust to injury-related losses in physical, cognitive, and social functioning. Individuals for whom anxiety improved in our study from 2 to 12 months post-injury may have experienced a reduction in distress caused by gains in function

Table 6. Multinomial Logistical Regression for Predictors of Depression Class Membership

	Class 1 (Stable minimal[a])		*Class 2 (Stable low)*		*Class 3 (Rapid worsening)*		*Class 4 (Delayed depression)*	
Variables	*Est (SE)*	*Mean (SD)*	*Est (SE)*	*Mean (SD)*	*Est (SE)*	*Mean (SD)*	*Est (SE)*	*Mean (SD)*
Sex[b]	–	1.23 (0.42)	0.15 (0.7)	1.27 (0.46)	0.49 (0.78)	1.33 (0.49)	**-26.04 (0)*****	**1 (0)**
Age	–	39.73 (16.88)	-0.02 (0.02)	37.6 (13.83)	-0.03 (0.02)	35.8 (15.9)	**-0.13 (0.05)***	**27.4 (8.44)**
Years of education	–	13.71 (3.15)	-0.02 (0.11)	13.53 (2.90)	**-0.22 (0.11)***	**12.33 (2.23)**	0.19 (0.34)	13.8 (3.19)
TBI severity[c]	–	0.003 (0.76)	-0.01 (0.45)	-0.03 (0.82)	-0.17 (0.42)	-0.14 (0.71)	0.70 (1.46)	0.27 (0.9)
Psychiatric history[d]	–	0.18 (0.39)	1.11 (0.74)	0.36 (0.5)	0.34 (1.08)	0.2 (0.41)	-0.14 (1.58)	0.2 (0.45)

Boldface represents statistically significant predictor.
[a]Stable minimal class served as the referent.
[b]Male = 1 and female = 2.
[c]TBI severity measured as an aggregate z-score of GCS, PTA, and length of acute care stay.
[d]0 = no and 1 = yes.
*$p < 0.05$; ***$p < 0.001$.
Est, estimate; SE, standard error; SD, standard deviation; TBI, traumatic brain injury; GCS, Glasgow Coma Scale; PTA, post-traumatic amnesia.

occurring during the earlier period of recovery,[32] at which time many clinical, employment, and social supports are still in place. Anxiety may then return and worsen from 12 to ≥36 months post-injury once recovery has slowed, and individuals are facing chronic impairments and changes to functioning, such as in relationship, social, and employment roles.[8,33]

Depression trajectories

To our knowledge, this study is the first to model trajectories of depression post-TBI for as long as ≥36 months post-injury. Similar to the anxiety trajectories, most individuals followed a pattern of stable minimal (70%) or mild (10%) BDI depression scores across time, replicating previous trajectory findings (in mild to severe patients) measured up to 24 months post-injury.[14–16] The remaining 20% of individuals in our study were classed into two subgroups that experienced moderate to severe depressive symptoms by ≥36 months post-injury: a rapidly worsening group that increased in depression symptoms across each time point (mean BDI = 9, 16, 23, 26 at T1–T4, respectively), and a delayed group that reported minimal depression symptoms across the 1st year followed by a large increase in scores, falling into the moderate-severe category at ≥36 months post-injury (mean BDI = 7, 7, 7, 29 from T1 to T4).

Delayed depression that develops after 1 year post-injury has been shown in other longitudinal studies.[16] These findings indicate that the greatest prevalence and severity of emotional distress occur in the chronic stages of injury. These findings highlight the importance of monitoring individuals beyond 1 year post-injury, at a time when most patients are no longer receiving rehabilitation for their brain injury, and symptoms may be missed. The findings also suggest the need for prophylactic strategies, particularly for those at greatest risk, as discussed in the following section.

Association between anxiety and depression trajectory groups

The present study found that most individuals who had stable, minimal-low anxiety also had stable, minimal-low depression (92%). Almost half (46%) of individuals with worsening anxiety also had worsening depression, consistent with previous reports of high comorbidity of anxiety and depression in the TBI population.[14]

Predictors of trajectories

Younger age was predictive of being in the worsening anxiety and delayed depression groups in the present study. This may be because younger adults perceive a bigger sense of loss to their identity and lifestyle from pre- to post-injury than do older adults, as younger adults are typically at a life stage during which there is a more rapid development in terms of employment, romantic relationships, and family life.[34,35] Perceived change in identity has been associated with depression post-TBI in previous studies.[36] Studies have also linked greater depressive symptoms to lower life satisfaction following moderate-severe TBI, and this relationship was associated with younger age.[37]

Delayed depression was also predicted by being male, and less education predicted rapidly worsening depression. Lower pre-injury educational level has been predictive of less post-traumatic growth in meta-analyses,[38] potentially because of a relationship between less education and less deployment of adaptive coping strategies.[39] Mechanisms through which these demographic factors predict worsening emotional distress up to 3 years post-injury should be further explored, as the present study is limited in its ability to explore mediators (e.g., coping strategies). Additionally, previous studies that have identified TBI severity to be predictive of emotional distress have included a wider range of severity, from mild to severe TBI. Therefore, the lack of association between TBI severity and psychological trajectories in the present study may be because of the smaller range of TBI severity.

Associations between trajectories and return to productivity

The association between psychological trajectories and return to productivity can contribute to an understanding of the clinical implications and potential mechanisms of these trajectories. Only 5% of individuals with worsening anxiety had returned to previous roles at home, work, or school by 1 year post-injury compared with 34% of those with stable, minimal-low anxiety. Similarly in the depression trajectories, although 20% of those with delayed depression had returned to previous roles by 1 year post-injury, only 8% of those with rapidly worsening depression had returned to productivity by 1 year, compared with 32% of those with stable, minimal-low depression. It is unclear from the present study whether return to productivity is a cause or consequence of anxiety and depression, though we speculate that it is likely to be both. Less participation in work and leisure activities has been shown to be associated with worsening life satisfaction among individuals with moderate to severe TBI at 1, 2, and 5 years post-injury.[37] A cross-lagged analysis study[40] found that functional changes 6 months post-TBI predicted 12-month anxiety and depression, but that anxiety and depression were not predictive of later functional status. These findings support the need for ongoing vocational rehabilitation and social programs, which may mitigate feelings of identity loss (by supporting return to or development of meaningful life roles) that will improve quality of life along with mood and anxiety.[37]

Limitations

The key limitations of the present research are as follows. First, the study employed self-report measures of anxiety and depression, which may be confounded by common method biases. Second, the ability to examine within-group differences was limited by the sample sizes of the smaller subgroups. For example, the dichotomization of variables such as return to productivity and psychiatric history may reduce their interpretive power. Further, although previous findings of participants from the parent study demonstrated that anxiety symptoms predicted hippocampal atrophy,[41] we did not use our imaging findings in the current study. Ninety percent of participants in the study had positive imaging findings, with heterogeneity of diffuse and focal lesions, atrophy of the whole brain and substructures, and progressive changes in volumes and cortical morphometry across time (as presented in previous studies).[42–45] Therefore, we considered the ability to utilize our neuroimaging findings as a predictor of trajectory outcome limited, particularly given our sample sizes. Future research should elaborate on the associations between anxiety and depression trajectories and their predictors, mediators, and consequences, including neurobiological and psychosocial factors.

Conclusion

The present study is one of the first to examine trajectories of anxiety and depression in moderate-severe TBI from the acute through chronic stages post-injury. Although most individuals reported stable, low levels of emotional distress over time, the use of LGMM allowed the identification of smaller subgroups of individuals for whom anxiety and depression followed different, worsening trajectories of growth. It is of clinical importance to highlight those individuals who have low levels of emotional distress in the 1st year post-injury, when they are most likely to be followed by healthcare services, but then experience substantially increased anxiety and depression in the chronic stages of recovery, particularly as increased mood disturbance is associated with suicidality. We identified predictors of worsening anxiety and depression, including younger age, less education, and male gender. These predictors may help target individuals at higher risk for later emotional distress. Additionally, findings that worsening anxiety and depression are associated with a lower likelihood to return to productivity by 1 year post-injury emphasize the importance of directing appropriate preventative measures, such as social supports and vocational rehabilitation, to improve mental health and functional outcomes. Further research is needed to determine the causal relationships between mood and anxiety trajectories and return to productivity. More broadly, further investigation is needed to identify the biological and psychosocial mechanisms that drive the growth of anxiety and depression across time in this population, to better inform interventions.

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Authors' Contributions

Laura M Heath was responsible for writing (lead) and data analysis (lead). M. Rafae Kidwai was responsible for data analysis (supporting), literature review, and writing – review and editing. Brenda Colella was responsible for conceptualization, study design, data collection, project administration, and writing – review and editing. Georges Monette was responsible for study design, data analysis (supporting), and writing – review and editing. Pavel Tselichtchev was responsible for writing (previous draft) and data analysis (previous draft). Jennifer C. Tomaszczyk was responsible for writing – review and editing. Robin E Green was responsible for conceptualization, study design, data collection, project administration, and writing – review and editing.

Transparency, Rigor, and Reproducibility Summary

The study and analysis plan were not formally preregistered, but the team member with primary responsibility for the analysis certifies that the analysis plan was pre-specified. The use of LGMMs precludes a straightforward *a priori* estimate of power. General recommendations support that a sample size of 50–100 participants is minimally sufficient to detect expected effects according to the analytical plan. There were 193 participants in the larger study and adequate data for the current study analyses were obtained from 148. Data analyses were performed by investigators blinded to participant identifying information. All questionnaires and software used to collect and examine the data are widely available. The key inclusion criteria and outcome evaluations are established standards. The handling of missing data and analytical decisions are described in the text and supplementary text.

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Author Disclosure Statement

No competing financial interests exist.

Supplementary Material

Supplementary Text

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