Prediction of Late-Onset Psychiatric Disorder in Survivors of Severe Injury:
Findings of a Latent Transition Analysis

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ABSTRACT

Objective: There is a growing body of evidence indicating that late or delayed onset of psychiatric disorder following traumatic injury and other psychological trauma is common. This research, however, has not examined factors that pose risks for delayed development of different types of psychopathology or at different time points. Such research has considerable implications for the development of screening, assessment, and intervention practices. This article investigates risk factors for late-onset disorders up to 72 months after a severe injury.

Methods: In this 6-year longitudinal study, 1,167 hospitalized patients with severe injury recruited between April 2004 and February 2006 were analyzed with repeated measures at 3, 12, and 72 months after injury. The Mini-International Neuropsychiatric Interview (MINI) and Clinician-Administered PTSD Scale (CAPS) were employed to complete diagnoses according to *DSM-IV*. Latent transition analyses with continuous covariates (injury severity, social support, recent life events, and pain) and 1 dichotomous covariate (presence/absence of a psychiatric disorder before injury) were conducted to identify risk factors for transitioning out of a No Disorder class and into one of 3 previously reported psychopathology classes (PTSD [posttraumatic stress disorder]/Depression, Alcohol/Depression, and Alcohol only) between 3 and 12 months (transition 1) and between 12 and 72 months (transition 2) postinjury.

Results: Movement into the PTSD/Depression class was predicted by injury severity at transitions 1 ($P = .003$) and 2 ($P = .017$) and social support ($P = .006$) at transition 1. Past psychiatric history increased the likelihood of moving into the PTSD/Depression class, with anxiety or mood disorders specifically implicated in transition 1. Movement into the Alcohol/Depression class was predicted by social support at transitions 1 ($P = .008$) and 2 ($P < .001$) and also by injury severity ($P < .001$) and pain ($P < .001$) at transition 2. Movement into the Alcohol class was predicted only by pain ($P = .011$) at transition 2. A history of a substance use or alcohol use disorder before injury was implicated in movement into both of the alcohol-based classes.

Conclusions: Predictors of developing a delayed-onset psychiatric disorder after severe injury differed by duration after injury and class of disorder. These findings highlight the need to offer targeted screening based on these risk factors to severe injury survivors up to 12 months postinjury, even when they present without disorder at 3 months.

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Research into psychiatric outcomes following accidental injury commonly addresses prevalence rates of and risk factors for acute disorder development and persistence.[1–5] While the acute phase is crucial to recovery, focusing solely on this stage risks missing those who present well initially but whose condition deteriorates over time.[6,7] Our previous research found that a substantial number of traumatic injury survivors presented with no psychiatric disorder in the first 3 to 12 months postinjury, but developed psychopathology at a later point.[8] This follow-up article investigates risk factors for late-onset disorder development.

A central question for clinical practice guidelines and health care systems is the role of posttrauma follow-up screening. Critically with growing evidence for late-onset development of disorders, what are the indications for follow-up in the absence of an initial disorder? In a study of posttraumatic stress disorder (PTSD) trajectories following a severe injury, deRoon-Cassini and colleagues[7] identified a delayed-onset typology in traumatic injury survivors exemplified by a sharp and dramatic increase in symptoms between 3 and 6 months postevent. A recent meta-analysis also found that 25% of trauma survivors who developed PTSD had a delayed onset.[9] The findings that some trauma survivors initially screen as asymptomatic or with low levels of symptoms, yet subsequently develop a disorder, suggest a need for targeted follow-up evaluations. There is currently a dearth of research to inform indications for follow-up psychiatric evaluations after injury and trauma.[10]

While PTSD is a well-recognized sequela of traumatic injury, the onset of other disorders such as mood, anxiety, and substance use disorders is also commonly reported.[1,5,11] To date, there has been limited research examining delayed onset for disorders other than PTSD. We have previously documented 4 latent classes of psychopathology that continue to present up to 72 months following injury.[8] These included 3 psychopathology classes—PTSD/Depression, Alcohol/Depression, and Alcohol only—and a No Disorder class. The psychopathology class structure that we identified demonstrated stability

Clinical Points

- There is substantial research into late-onset disorders after a traumatic event. However, there is a dearth of research that helps identify risk factors for a late-onset disorder.
- Predictors of developing a delayed-onset psychiatric disorder after severe injury differed by duration after injury and by types of disorder clusters.
- The results suggest that social support, pain, injury severity, and preinjury psychiatric history may be included in targeted follow-up procedures for survivors of traumatic injury.

and invariance across the time points of 3, 12, and 72 months postinjury. Despite this stability, migration across the classes was evident, with several trauma survivors migrating from the No Disorder class into one of the 3 psychopathology classes at 12 and 72 months. At 12 months, 29% of those in a disorder-based class had reported no disorder at 3 months, and 18% of those presenting with psychopathology at 72 months presented without disorder at 12 months. Consistent with the meta-analysis by Utzon-Frank and colleagues,[9] our research observed that a sizable proportion, approximately one quarter, of traumatic injury survivors who develop a disorder do so in the postacute phase.

These findings highlight the need to better identify those presenting without disorder at 3 or 12 months who are at specific risk to develop psychopathology over time. Without such identification, the needs of these injury survivors are likely to remain unrecognized, with the result that they may not receive appropriate support.

While it would be possible to recommend routine follow-up assessments for all trauma survivors to reduce the risk of missing delayed-onset pathology, this would be cost-prohibitive.[1,7] Therefore, it is critical to identify who is most at risk for developing a disorder in the postacute phase and to target follow-up screening and monitoring accordingly.

A growing body of research has examined potential risk factors for development of psychopathology following severe injury. The factors most commonly reported include a history of psychopathology prior to the injury,[12] injury severity,[13] current level of pain,[14] presence of positive social support,[15,16] and subsequent stressful events.[17,18] Research that examines the impact of these risk factors on the development of disorder in the postacute phase can provide guidance to clinical services regarding monitoring of injury survivors over time. Hence, in the current study, we built on previously reported findings of latent psychopathology classes over time to investigate risk factors associated with migration into one of the psychopathology classes at 12 months and at 72 months postinjury following categorization in the No Disorder class at 3 and 12 months, respectively.

METHODS

Participants were 1,167 injury patients who were admitted to the trauma service of one of 4 major Australian trauma hospitals for at least 24 hours between April 2004 and February 2006 and met the *DSM-IV* Criterion A1 for PTSD. Participants were recruited provided they had a reasonable understanding of English, were not currently psychotic or suicidal, and did not have a traumatic brain injury (TBI) that was more severe than mild using the American Congress of Rehabilitation Medicine definition.[19] All participants provided written informed consent. The research was approved by the Human Research and Evaluation Committee (HREC) in each hospital. See Forbes et al[8] for more details on the sample.

Measures

Posttraumatic stress disorder was assessed using the Clinician Administered PTSD Scale (CAPS),[20] which has demonstrated excellent reliability and validity.[21] The Mini-International Neuropsychiatric Interview version 5.5 (MINI),[22] a structured diagnostic interview based on *DSM-IV* and *ICD-10* classifications of psychopathology with good diagnostic reliability for all diagnoses compared to the Composite International Diagnostic Interview,[22] was used to identify major depressive episode, panic disorder, agoraphobia without panic, obsessive-compulsive disorder (OCD), social phobia, generalized anxiety disorder (GAD), alcohol abuse, and alcohol dependence. For fidelity data, see Forbes et al.[8]

Information regarding the injury (eg, injury severity, mild TBI) and the admission (eg, length of stay) was obtained from the hospital files. Injury severity was assessed using the Injury Severity Scale (ISS).[23]

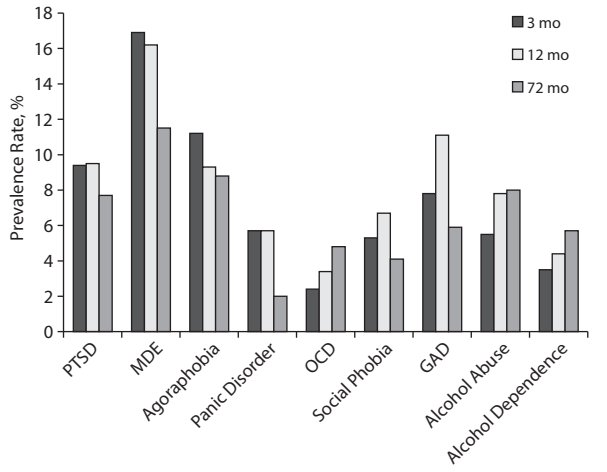
Participants were asked about the occurrence of common life events that may be deemed threatening. The Recent Life Events questionnaire was adapted from Brugha and colleagues[24] with 9 additional items included.

The Schuster social support questions[25] were used to identify positive social support provided by friends and family. Pain was measured using a simple Visual Analog Scale,[26] which is considered to be a reliable and change sensitive measure of the subjective experience of pain severity.[27]

Statistical Analyses

The analyses for this article are a follow-up to the latent transition analysis (LTA) previously reported. For information on the procedure followed to define the number of classes at each time point and to structure the transition parameters, see the earlier article by Forbes et al.[8] Importantly, that study identified 4 classes as previously outlined: No Disorder, PTSD/Depression, Alcohol, and Alcohol/Depression (in decreasing order of size across the time points). Five theoretically derived covariates were assessed as potential predictors of transition from the No Disorder class into each of the disorder-based classes, namely, injury severity, positive social support, pain, and recent life events measured as continuous variables and diagnosis of a psychiatric disorder prior to injury (called past psychiatric history hereafter) measured as a dichotomous variable. Social support, recent life events, and pain were

Figure 1. Prevalence Rates of Psychiatric Diagnoses at 3 (n = 987), 12 (n = 862), and 72 (n = 613) Months After Injury[a]



[a]Rates from Forbes et al.[8]
Abbreviations: GAD = generalized anxiety disorder, MDE = major depressive episode, OCD = obsessive-compulsive disorder, PTSD = posttraumatic stress disorder.

Table 1. Injury Severity (as indicated by ISS score), Positive Social Support, Pain, and Stressful Events as Predictors of Transition From the No Disorder Class at 3 Months Into Each Disorder Class at 12 Months[a]

Predictor	β	SE	*P*
PTSD/Depression class			
ISS score	**0.082**	**0.027**	**.003**
Positive social support	**–0.274**	**0.100**	**.006**
Pain	**0.382**	**0.149**	**.010**
Stressful events	0.163	0.156	.296
Alcohol/Depression class			
ISS score	0.061	0.052	.242
Positive social support	**0.254**	**0.095**	**.008**
Pain	0.165	0.343	.631
Stressful events	0.632	0.395	.110
Alcohol class			
ISS score	–0.041	0.031	.188
Positive social support	–0.110	0.083	.189
Pain	0.126	0.082	.121
Stressful events	0.023	0.115	.843

[a]β weights are unstandardized; significant results are displayed in boldface.
Abbreviations: ISS = Injury Severity Scale, PTSD = posttraumatic stress disorder.

all assessed at each time point in relation to the patients' experiences in the intervening period between time points. A review of these covariates found that all have low levels of multi-colinearity, which supports simultaneous analyses.

Mplus version 7.02 was employed for the analysis.[28] Full information maximum likelihood estimation was used to adjust for missing data on latent class indicator variables. The robust maximum likelihood estimator was employed for the analyses. Multiple imputation was conducted in Mplus to account for missing values on covariates. LTA models for 2 time points with covariates influencing the latent transition probabilities were run. This analysis measures how well each covariate predicts the transition from a class at time 1 into a class at time 2. The output in Mplus provides β weights and *P* values using the specified covariate as the predictor and the transition parameter as the outcome. This study is concerned with 3 transition parameters: (1) No Disorder to PTSD/Depression, (2) No Disorder to Alcohol, and (3) No Disorder to Alcohol/Depression.

Analyses involved 4 steps. Firstly, the 4 continuous covariates were assessed simultaneously as potential predictors of those who transitioned out from the No Disorder class at 3 months into each of the 3 psychopathology-based classes at 12 months (transition point 1). These analyses assessed the ability of a covariate to predict the transition between specific classes from time 1 to time 2 (ie, to predict the transition parameter), not the capacity of a covariate to predict an individual's class membership at time 1 or time 2. Secondly, the same analyses were completed for those transitioned out of No Disorder at 12 months into 1 of the 3 psychopathology based classes at 72 months (transition point 2).

In step 3 and step 4, the presence of a past psychiatric history was assessed as a predictor for transition point 1 and transition point 2, respectively. With a binary covariate, the Mplus output provides conditional probabilities for each covariate value. For the purpose of our study, this represents the conditional probability of transition should the participants have past psychiatric history status of "No" and a comparative conditional probability of transition should the participants have a past psychiatric history status of "Yes." This output can be used to generate odds ratios that may be compared, although not statistically tested.

RESULTS

See Figure 1 for prevalence rates of psychiatric diagnoses at 3, 12, and 72 months after injury.

Transition Point 1: 3 Months to 12 Months

At 3 months, there were 812 people in the No Disorder class. At 12 months, 63 had transitioned into one of the psychopathology classes: 28 into PTSD/Depression, 32 into Alcohol, and 3 into Alcohol/Depression. These 63 represented 29% of those presenting in the psychopathology classes at 12 months. As can be seen in Table 1, higher injury severity scores, lower positive social support, and higher pain scores predicted movement into the PTSD/Depression class at 12 months compared to those who remained in the No Disorder class. Table 1 also shows that positive social support predicted movement into the Alcohol/Depression class at 12 months, but in this case, higher scores of positive social support were predictive of the transition. None of the 4 continuous predictors identified transition into the Alcohol class.

Injury survivors who transitioned from No Disorder into the PTSD/Depression class were 3.28 times more likely to have a psychiatric disorder prior to injury. A review of the disorder types found that 15 (63%) of the 24 who transitioned into the PTSD/Depression class had a history of an anxiety or mood disorder. No calculation of odds ratios

Table 2. Injury Severity (as indicated by ISS score), Positive Social Support, Pain, and Stressful Events as Predictors of Transition From the No Disorder Class at 12 Months Into Each Disorder Class at 72 Months[a]

Predictor	β	SE	*P*
PTSD/Depression class			
ISS score	**0.083**	**0.035**	**.017**
Social support	−0.053	0.251	.832
Pain	0.734	0.473	.121
Stressful events	0.135	0.088	.126
Alcohol/Depression class			
ISS score	**0.286**	**0.079**	**<.001**
Social support	**−1.042**	**0.245**	**<.001**
Pain	**1.591**	**0.409**	**<.001**
Stressful events	−1.253	0.836	.134
Alcohol class			
ISS score	0.010	0.046	.829
Social support	−0.101	0.083	.223
Pain	**0.401**	**0.158**	**.011**
Stressful events	0.141	0.085	.098

[a]β weights are unstandardized; significant results are displayed in boldface.
Abbreviations: ISS = Injury Severity Scale, PTSD = posttraumatic stress disorder.

was permissible for transition into either of the alcohol-based classes as every injury survivor who migrated into this class had a history of a disorder prior to injury. A review of the types of psychiatric disorders present before injury found that 30 (88%) of the 34 who transferred from No disorder into one of the alcohol-based classes had a history of either an alcohol-based disorder or another substance use disorder. The remaining 4 (12%) had a history of an anxiety or mood disorder.

Transition Point 2: 12 Months to 72 Months

At 12 months, there were 769 people in the No Disorder class. At 72 months, 32 of these people had transitioned into one of the psychopathology classes; 6 into PTSD/Depression, 24 into Alcohol, and 2 into Alcohol/Depression. These 32 individuals represented 18% of the total sum in the psychopathology classes. As can be seen in Table 2, the covariates that predict transition into a specific disorder class at 72 months are quite different from those observed at 12 months. Table 2 shows that, at 72 months, higher injury severity was the only significant predictor of movement into the PTSD/Depression class compared to retention in the No Disorder class. Positive social support and pain were no longer significant predictors of migration from No disorder into the PTSD/Depression class. Transition into the Alcohol/Depression class was predicted by higher injury severity, less positive social support, and higher subjective pain scores. Transition into the Alcohol class was predicted only by higher subjective pain scores.

Injury survivors who transitioned from No Disorder into the Alcohol class were 1.16 times more likely to have had a psychiatric disorder prior to injury. A review of the types of psychiatric disorders found that 10 (67%) of the 15 who transitioned into the Alcohol class had a history of a substance use or alcohol use disorder. Those who transitioned into the PTSD/Depression class were 0.5 times as likely (ie, were less likely) to have a psychiatric history. Therefore, a person with a previous psychiatric history was more than twice as likely (2.32 times) to transition into the Alcohol class than into the PTSD/Depression class. Both participants who transitioned from No Disorder at 12 months into the Alcohol/Depression class at 72 months had a history of a substance use disorder (but not alcohol use disorder).

DISCUSSION

Two important conclusions can be drawn from these analyses. First, factors that predict development of psychopathology in the postacute phases vary across time points. Predictors of transition into a psychopathology class between 3 and 12 months (transition 1) are different from those between 12 and 72 months (transition 2). Second, these predictors vary depending upon which disorder class a person transitions into, with different predictors for transition to the Alcohol, Alcohol/Depression, and PTSD/Depression classes. These findings build the case for targeted follow-up procedures for survivors of traumatic injury.

Specifically, this study found that a more severe injury was associated at both transition points with a greater risk for those without disorder moving into the PTSD/Depression class. These findings suggest that clinicians need to be aware that, in the postacute phase, those with more severe injury, even if presenting without psychiatric disorder at 3 or 12 months postinjury, are still at risk for development of PTSD and depression.

Transition into the PTSD/Depression class was also predicted by low positive social support and self-reported pain at transition point 1, but not at transition point 2. For those individuals for whom social support is an important protective factor, its absence will likely contribute to psychopathology in the first 12 months. If the absence of social support has not contributed to psychopathology after the first 12 months, it is unlikely to do so. These individuals presumably employ other coping mechanisms that do not rely on social support. Similarly, the findings in relation to pain suggest that those individuals for whom pain is going to contribute to psychopathology will develop a disorder within the first 12 months. If pain has not contributed to psychopathology within the first 12 months, it is unlikely to do so. Those in the No Disorder class at 12 months with more severe ratings of pain may have adapted in such a way as to prevent its risk of precipitating subsequent psychiatric disorder.

Social support predicted movement into the Alcohol/Depression class at both transition points but, interestingly, in opposite directions. In the first transition, higher levels of positive social support predicted movement, whereas in the second transition, lower levels of positive social support were predictive. In understanding the former finding, it may be that, in the postacute phase, social support effectively facilitates alcohol consumption at a recreational level for some individuals and is possibly also used to self-medicate depressive symptoms. This is in contrast to the finding reported above that high positive social support is

protective against movement into the PTSD/Depression class at transition point 1. Taken together, these findings highlight the need to carefully assess the nature and function of social support in considering its role in facilitating or impeding recovery for a given individual. Given that at transition point 2, only 2 participants moved from no disorder into the Alcohol/Depression class, it is premature to speculate on factors underlying this transition.

Movement into the Alcohol class was predicted by higher levels of pain at transition point 2. However, at both transition points there was a history of a substance use (often alcohol) disorder prior to injury for those who moved into either of the alcohol-based classes. This finding suggests that individuals who have a history of substance use are at risk for relapse, using substance use as a coping mechanism when difficulties arise in their recovery process.

A past psychiatric history increased the likelihood of transition into the PTSD/Depression class between 3 and 12 months, but decreased the likelihood between 12 and 72 months. At the first transition point, the clear majority of those who moved into the PTSD/Depression class had a history of a mood or anxiety disorder. This finding again indicates that, even when presenting without disorder 3 months postinjury, a preinjury history of anxiety or mood disorder may indicate a risk for later onset adaptation problems.

Overall, injury severity in conjunction with a preinjury psychiatric disorder is an important predictor of delayed-onset disorders. Importantly, the disorders that develop postinjury are related to the preinjury diagnoses. Individuals with more severe injuries who had an anxiety or mood disorder preinjury were at risk of moving into the PTSD/Depression class, whereas individuals with more severe injuries who had a substance use disorder preinjury were more likely to move into the Alcohol or Alcohol/Depression classes. Additionally, those with preinjury alcohol use or substance use disorders who reported increased levels of pain were at specific risk for developing a disorder in the Alcohol or Alcohol/Depression class.

The results of this study need to be interpreted with some caution given the low numbers of participants migrating from No Disorder to one of the psychopathology groups. Clearly, it will be important to replicate these findings with larger datasets, perhaps using international collaborations. Nevertheless, these findings have important preliminary implications for clinical service delivery across screening, assessment, and clinical interventions. First, initial screening and assessment practices need to include collation of a comprehensive psychiatric history. Second, injury survivors with a history of psychiatric disorder—particularly anxiety, mood, and substance use disorder—higher injury severity, and self-reported pain should be offered follow-up screening. Collaborative care[29] and stepped care[30] models that provide ongoing medical and psychological support may benefit from targeted screening practices employing these measures. Third, interventions should be targeted across disorders to take account of the co-occurrence of disorders within classes. Fourth, the presence of social support may not be sufficient to predict recovery. The nature and function of social support should be assessed. Finally, consideration should be given to brief prevention-focused interventions to boost coping resources for those with risk factors identified here but presenting without disorder at 3 months. These interventions have the potential to improve management of the difficulties associated with recovery following traumatic injury and prevent development of psychiatric disorder in those at risk.

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