

Prospective comparison of acute confusion severity with duration of post-traumatic amnesia in predicting employment outcome after traumatic brain injury

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Background: Measurement of the duration of post-traumatic amnesia (PTA) is common practice, serving as an important index of the severity of traumatic brain injury (TBI) and a predictor of functional outcome. However, controversy exists regarding the nature of PTA; some studies indicate that it is a confusional state with symptoms that extend beyond disorientation and amnesia.

Objective: To evaluate the contribution of the severity of acute confusion 1 month after TBI to prediction of employment at 1 year after injury, comparing it with PTA duration.

Methods: Prospective study involving 171 participants with complete data, who met the study criteria, from 228 consecutive TBI Model System admissions. Outcome measures included weekly administration of the Delirium Rating Scale-Revised-98 (DelRS-R98) to measure the severity of acute confusion. Evaluations closest to 1 month after injury were used for study purposes. Duration of PTA was defined as the interval from injury until two consecutive Galveston Orientation and Amnesia Test scores of ≥ 76 were obtained within a period of 24–72 h. Univariable and multivariable logistic regression were used to predict employment status at 1 year after injury.

Results: Age, education and DelRS-R98 were significant predictors accounting for 34% of outcome variance. Individuals with greater confusion severity at 1 month after injury, older age and lower levels of education were less likely to be employed at 1 year after injury. Severity of confusion was more strongly associated with employment outcome ($r_s = -0.39$) than was PTA duration ($r_s = -0.34$).

Conclusions: In addition to demographic indices, severity of acute confusion makes a unique contribution to predicting late outcome after TBI.

Impaired consciousness represents the clinical hallmark of non-penetrating traumatic brain injury (TBI).^{1,2} Individuals with mild TBI may experience a brief period of confusion, while others with greater injury severity may become comatose followed by prolonged confusion with amnesia.² This transitory state of impaired consciousness is commonly referred to as post-traumatic amnesia (PTA). Determination of the duration of PTA is important as it yields an index of injury severity and is one of the best predictors of recovery and functional outcome.^{3–7} Prospective evaluation of PTA is common practice in rehabilitation settings, largely because it provides an ongoing index of the patient's progress³ and suitability for neuropsychological testing.^{7,8}

Historically, investigations of PTA primarily focus on the disorientation and amnesic aspects of impaired consciousness after TBI, yet other neurobehavioral manifestations commonly occur. Stuss *et al* found that attentional disturbance is a key aspect of impaired consciousness among confused patients with TBI.⁹ They noted similarities between post-traumatic impaired consciousness and delirium, a confusional state in which attentional deficits are commonly observed. They further proposed that the term "post-traumatic confusional state" replace the more commonly used "post-traumatic amnesia" as PTA less accurately represents cognitive impairments after TBI.⁹ Similarly, Nakase-Thompson *et al* and later Sherer *et al* studied confusion among neurorehabilitation admissions with TBI and found that traditional measures of PTA did not adequately reflect the range of observed neurobehavioral impairments.^{10,11} In addition to attentional, orientation and memory impairments, prevalent manifestations found among confused

patients after TBI included sleep-wake cycle disturbance, decreased daytime arousal, fluctuation in cognitive and behavioural symptom severity, motor agitation, affective lability, and perceptual and thought process abnormalities.^{10,11}

Studies addressing PTA as a predictor of outcome typically examine duration; that is, the time elapsed from injury until meeting a criterion for return of orientation and/or memory.^{12–15} Important methodological limitations exist, however, in the determination of PTA duration.^{3,16,17} While the early stages of PTA are easily recognised, identifying the end point is more challenging.^{16–18} In some cases, patients are no longer available for determination of PTA emergence, having been transferred to home or another setting. Conversely, PTA resolution may occur prior to the initial evaluation, requiring retrospective estimation. Furthermore, different PTA measures may yield discrepant PTA duration recordings in the same patient, raising questions of test validity.^{3,17,19,20} As duration of PTA is influenced by injury severity, evaluating the severity of confusion at a set time after injury potentially reduces the confounding influence of evaluation results with those of duration of TBI recovery.

In an effort to clarify the relevance of severity, rather than duration of confusion symptoms, after TBI on functional outcome, we examined the predictive utility of a measure that encompasses many aspects of neurobehavioral impairment associated with acute confusion. We hypothesised that a rating

Abbreviations: DDC, delirium diagnostic criteria; DelRS-R98, Delirium Rating Scale-Revised-98; GCS, Glasgow Coma Scale; GOAT, Galveston Orientation and Amnesia Test; IRC, interquartile range coefficients; PTA, post-traumatic amnesia; TBI, traumatic brain injury

scale that evaluates the range and severity of behavioural, cognitive and physiological changes associated with early confusion will provide unique utility in predicting late functional outcome. Moreover, clinicians caring for persons with TBI whose contacts with patients are too limited in time to permit determination of PTA duration could still have useful prognostic information. This study primarily aimed to examine the nature and severity of acute confusion utilising a common measure in the delirium literature, the Delirium Rating Scale-Revised-98 (DelRS-R98),²¹ at 1 month after TBI, and its relationship to employment outcome at 1 year after injury. The second aim was to compare the functional prognostic value of the 1 month DelRS-R98 with that of PTA duration, as assessed by the Galveston Orientation and Amnesia Test (GOAT),²² a common measure of PTA.^{16 19}

METHOD

Study population

The study population comprised all TBI Model Systems participants admitted to a free standing neurorehabilitation hospital from January 1999 to December 2003. Criteria for the National Institute on Disability and Rehabilitation Research TBI Model Systems programme include: (1) medically documented TBI; (2) treatment at an affiliated level I trauma centre within 24 h of injury; (3) receipt of inpatient rehabilitation within the model system; (4) admission to inpatient rehabilitation within 72 h of discharge from acute care; (5) aged at least 16 years at the time of injury; and (6) provision of informed consent by the person with injury or a legal proxy.²³ Patients who were in a minimally conscious state²⁴ or vegetative state at 1 month after injury were excluded from the current investigation. Individuals were also excluded from the study if they: (1) had a severe premorbid neurological disorder, (2) were retired or unemployed and not looking for work at the time of injury or (3) had missing information regarding the severity of the injury.

Data collection procedures

Research assistants collected information on demographic characteristics (sex, race, years of education, age, pre-injury employment status), cause of injury, injury severity (Glasgow Coma Scale (GCS) scores) at admission to the emergency department, duration of PTA and length of stay (acute care, rehabilitation), from hospital and emergency medical service records and from interviews with participants and their family members. PTA was defined as the interval from injury until two consecutive GOAT scores of ≥ 76 were obtained within a period of 24–72 h.²⁵ For individuals who did not resolve PTA during rehabilitation hospitalisation, duration of PTA was estimated based on duration of coma using a formula developed by Katz and Alexander¹² or rehabilitation length of stay plus 1 day.

On a weekly basis, a neuropsychologist rated each participant on the DelRS-R98²¹ and determined whether the participant met Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition diagnostic criteria for delirium.²⁶ Delirium diagnostic criteria (DDC) include: (A) disturbance of consciousness with attentional impairment, (B) change in cognition or development of a perceptual disturbance not attributable to dementia, (C) disturbance develops over a short period of time and fluctuates during the course of the day and (D) disturbance is caused by a general medical condition. Finally, the time elapsed since injury (in days) was coded for each weekly observation. Evaluations obtained closest to 1 month after injury were used for this study. Individuals were contacted using in-person interviews or telephone follow-up at approximately 1 year after injury (range 10–14 months) to collect data on employment status.

Measures

Delirium Rating Scale-Revised-98

The DelRS-R98 is a 16 item clinician rating scale that includes 13 severity items and 3 diagnostic items of delirium.²¹ Individual items assess temporal onset of symptoms, perceptual disturbance, delusions, psychomotor behaviour, aspects of cognition (attention, language, visuospatial disturbance, short term memory and long-term memory), presence of a physical disorder accounting for symptoms, sleep-wake cycle disturbance, thought process abnormalities, lability of mood and fluctuation of symptoms. Ratings are determined by the presence and severity of symptoms. Item scores are summed to obtain a total score that may range from 0 to 46 (severity and diagnostic items summed) or 0 to 39 for the severity items only. The DelRS-R98 has excellent reliability, with a Cronbach's coefficient alpha of 0.90. Inter-rater reliability is excellent, with intraclass correlation coefficients ranging from 0.98 to 0.99. Trzepacz *et al* found that the DelRS-R98 successfully discriminated patients with delirium from patients with dementia, schizophrenia, depression and other mixed groups.²¹ Severity scores greater than 15 have demonstrated excellent specificity (93%) and sensitivity (92%) in these samples.²¹

Galveston Orientation and Amnesia Test

The GOAT is a 10 item measure that assesses orientation as well as memory for events preceding and following TBI. Areas of orientation include biographical information, place, time and current circumstances. Error points are assigned for incorrect response to items. Total error scores can range from 0 to 108, with higher error scores indicating poorer orientation. Error scores are subtracted from 100 to determine a GOAT score. Inter-rater reliability has been found to be excellent (correlation coefficient = 0.99).²² The GOAT has been used to determine the duration of PTA in numerous studies of TBI.^{16 25}

Analyses

Descriptive statistics (percentages, quartiles) for participant characteristics (age, sex, race, years of education, marital status, cause of injury) and injury severity (GCS score, PTA, and acute and rehabilitation lengths of stay) were calculated for participants and for potential participants who were excluded. Mann-Whitney tests and analysis of variance were used for comparing non-study and study subjects for age, education, GCS, PTA duration, and acute and rehabilitation lengths of stay.

Multivariable logistic regression analysis was used to test the hypothesis regarding prediction of employment at 1 year after injury from demographic variables (age, education), injury severity indices (GCS, PTA duration) and DelRS-R98. Univariable logistic regression analyses were also calculated to permit examination of unadjusted effects for each predictor. Effects for logistic analyses were reported as interquartile range coefficients (IRCs). IRCs indicated the odds of a participant at the 75th percentile on a predictor being used at follow-up compared with a participant at the 25th percentile on the predictor. Associations between variables of interest were examined using Spearman correlation coefficients (r_s). All calculations were performed using SPSS software, version 11.0. All statistical tests used two sided tests of significance with an alpha level of 0.05.

RESULTS

During the study period, 228 potential participants were enrolled in the TBI Model Systems programme. Of these, 23 did not emerge from a vegetative state or minimally conscious state and were excluded from the study. Thirteen potential participants were retired from work at the time of injury and

Table 1 Descriptive information for the study sample compared with patients not eligible for the study (n = 191)

	Study sample (n = 171)	Lost to follow-up (n = 20)
Sex (n (%))		
Male	120 (70)	18 (90)
Female	51 (30)	2 (10)
Race (n (%))		
White	108 (63)	11 (55)
African-American	61 (35)	9 (45)
Hispanic	2 (0)	0 (0)
Years of education (quartiles*)	10/12/13	9/12/12
Cause of injury (n (%))		
Motor	136 (80)	9 (45)
Fall	14 (8)	4 (20)
Blunt injury	9 (5)	2 (10)
Gun shot wound	8 (4)	1 (5)
Pedestrian	1 (1)	2 (10)
Hit/fly object	3 (2)	0 (0)
Other	0 (0)	0 (0)
Unknown		2 (10)
Marital status (n (%))		
Married	53 (31)	8 (40)
Single	99 (58)	5 (25)
Other†	19 (11)	7 (35)
GCS ED admit (n (%))		
3–8	117 (68)	10 (50)
9–12	31 (19)	3 (15)
13–15	23 (13)	6 (30)
Missing		1 (5)
PTA duration (quartiles)‡	19/31/54	18/31/74
Age (quartiles)	21/28/42	29/46/62
Acute LOS (quartiles)	15/22/32	11/20/35
Rehab LOS (quartiles)	14/20/30	14/23/40

Acute LOS, length of stay for acute hospitalisation; GCS ED Admit, Glasgow Coma Score at admission to the emergency department; PTA duration, duration of post-traumatic amnesia; Rehab LOS, length of stay for inpatient rehabilitation.

*Quartiles correspond to the 25th/50th/75th percentiles.

†The "Other" category includes widowed, divorced or separated.

‡Lost to follow-up sample included 18 persons for the descriptive information for PTA because of missing information for duration of unconsciousness and PTA.

thus were excluded from the study. One additional person was excluded because of profound aphasia resulting in missing information for duration of consciousness and PTA. Of the remaining 191 qualified participants, 20 were lost to follow-up (5 deceased, 15 unable to be contacted). These 20 participants (10%) were missing the study outcome, employment status at 1 year after injury and were excluded from the study. A comparison of descriptive information for the 171 study participants and the 20 subjects who were lost to follow-up is shown in table 1. Study participants were younger ($F = 18.02$; $p < 0.001$) and had lower admission GCS scores ($U = 1257.000$, $p = 0.05$) but no significant differences were found for years of education, PTA duration or length of stay between the two groups. There were 36 participants (21%) who did not resolve PTA prior to discharge from inpatient rehabilitation. Estimated durations of PTA were calculated for these individuals using the Katz and Alexander¹² formula and these values were used in all subsequent analyses. For seven individuals, the Katz and Alexander formula resulted in PTA duration estimates that were shorter than the known shortest possible duration, as indicated by total hospital length of stay. For these seven participants, total hospital length of stay plus 1 day was used as a conservative estimate of PTA duration.

Participants' DelRS-R98 ratings were collected a median of 30 days after injury, but observations ranged from 7 to 82 days post-injury because of short acute and rehabilitation hospital lengths of stay for some participants and long acute hospital

Table 2 Frequency of positive symptoms on the DelRS-R98 and percentage still with post-traumatic amnesia for the study sample (n = 171)

	DDC+ (n = 78)	DDC- (n = 93)
DelRS-R98 items		
Item 1. Sleep-wake cycle disturbance	45 (58%)	19 (20%)
Item 2. Perceptual disturbance	22 (28%)	01 (01%)
Item 3. Delusions	20 (26%)	01 (01%)
Item 4. Lability of affect	41 (53%)	16 (17%)
Item 5. Language	52 (67%)	29 (31%)
Item 6. Thought process abnormality	55 (70%)	15 (16%)
Item 7. Motor agitation	56 (72%)	23 (25%)
Item 8. Motor retardation	35 (45%)	27 (29%)
Item 9. Orientation	59 (76%)	23 (25%)
Item 10. Attention	71 (91%)	44 (47%)
Item 11. Short term memory	73 (94%)	70 (75%)
Item 12. Long term memory	71 (91%)	55 (59%)
Item 13. Visuospatial ability	60 (77%)	46 (49%)
Diagnostic items		
Item 14. Temporal onset	78 (100%)	92 (99%)
Item 15. Fluctuation of symptoms	71 (91%)	20 (22%)
Item 16. Physical disorder present	79 (100%)	93 (100%)
No in PTA by TBIMS GOAT criteria*	66 (85%)	28 (30%)

DDC+, delirium diagnostic criteria positive; DDC-, delirium diagnostic criteria negative; DelRS-R98, Delirium Rating Scale-Revised-98; GOAT, Galveston Orientation Amnesia Test; PTA, post-traumatic amnesia; TBIMS, Traumatic Brain Injury Model System.

*TBIMS PTA was defined as the interval from injury until two consecutive GOAT scores of ≥ 76 were obtained within a period of 24–72 h.²⁵

lengths of stay for others. For 136 participants (79%), DelRS-R98 scores were collected within 2 weeks of the 1 month injury target. Table 2 presents the frequency of confusion related symptoms, as measured by the DelRS-R98. The study sample is divided into those meeting DDC (DDC+) and those not meeting DDC (DDC-). Seventy-eight persons met DDC at 1 month after injury (46%) and 93 did not. Some symptoms (perceptual disturbance, delusions, thought process abnormalities) were much more common in participants meeting DDC while others (memory impairment, visuospatial impairment, impaired attention) were common in both groups.

Examination of employment status at 1 year after injury revealed that 51 participants (30%) were employed and 120 were not. Univariable logistic regression analyses were performed for each predictor (age, years of education, GCS, PTA and DelRS-R98) with employment at 1 year after injury as the outcome variable. Results of regression analyses showing unadjusted (univariable) effects are presented in table 3. Univariable logistic regression analyses revealed that age, years of education, PTA and DelRS-R98 were significant predictors of employment at 1 year after injury. Examination of unadjusted effects (IRCs) for these predictors indicated that participants at the 75th percentile of age (42.3 years) had 0.45 times the odds of being employed as participants at the 25th percentile of age (20.9 years). Stated another way, participants at the 25th percentile were over twice as likely to be employed at follow-up as those at the 75th percentile. Participants at the 75th percentile of education (13 years) had 2.08 times the odds of being employed at follow-up as participants at the 25th percentile (10 years). Participants at the 75th percentile (54 days) for PTA duration were only 0.35 times as likely as those at the 25th percentile (19 days) to be employed at follow-up. Stated another way, participants at the 25th percentile for age were almost three times as likely to be employed as those at the 75th percentile. Finally, participants at the 75th percentile (19) on the DelRS-R98 were only 0.20 times as likely to be employed as those at the 25th percentile (5). Stated another way, those at the 25th percentile of severity of confusion were

Table 3 Logistic regression models for predicting employment at 1 year after injury (n = 171)

Predictor	25th, 75th percentile comparison	Unadjusted effect* (95% CI)	p Value	Adjusted effect* (95% CI)	p Value
Age (y)	20.9, 42.3	0.45 (0.24, 0.85)	0.011	0.33 (0.15, 0.73)	0.006
Education (y)	10, 13	2.08 (1.35, 3.22)	0.001	2.48 (1.47, 4.19)	0.001
GCS	5, 10	1.23 (0.78, 1.96)	0.378	0.77 (0.57, 1.04)	0.385
PTA	19, 54	0.35 (0.20, 0.61)	0.001	0.63 (0.34, 1.18)	0.165
DelRS-R98	5, 19	0.20 (0.10, 0.41)	0.001	0.35 (0.14, 0.87)	0.023

DelRS-R98, Delirium Rating Scale-Revised-98; GCS, Glasgow Coma Scale at emergency department admission; PTA, duration of post-traumatic amnesia (days).

*All effects are interquartile range coefficients (IQR). IQR coefficients are the effects (changes in probability of employability) of increasing each predictor variable from its lower quartile (25th percentile) to its upper quartile (75th percentile).

five times as likely to be employed as those at the 75th percentile.

Multivariable logistic regression was performed with all predictors and employment at 1 year after injury as the outcome variable. Results are shown in table 3. The multivariable full model was reliable ($\chi^2 = 47$, $df = 5$, $p < 0.001$). The model accounted for approximately 34% of the variance in employment status at 1 year after injury. Age, education and severity of confusion (DelRS-R98) each made unique contributions to prediction of employment at the 1 year follow-up after adjustment for all other predictors. The adjusted effect for age was larger than the unadjusted effect, with participants at the 25th percentile three times as likely to be employed as those at the 75th percentile. The effect for education was also stronger in the adjusted model, with those at the 75th percentile having 2.48 times the odds of being employed at follow-up compared with those at the 25th percentile. Unlike the unadjusted effect, the adjusted effect for PTA duration was not significant. The adjusted effect for DelRS-R98 was moderated, with participants at the 75th percentile almost 0.35 times as likely to be employed as those at the 25th percentile. Stated another way, participants who were less confused were almost three times as likely to be employed as those who were more confused. The failure of PTA duration to make a significant contribution to prediction in the multivariable analysis was likely due to the strong association of severity of confusion with PTA ($r_s = 0.75$). Correlational analyses also demonstrated that severity of confusion was more strongly associated with employment outcome ($r_s = -0.39$) than was PTA with employment outcome ($r_s = -0.34$). The same analyses were completed on the subset of 136 participants for whom DelRS-R98 data were collected within a 2 week window of the 30 day post injury target. Findings from these analyses were essentially identical to analyses for the full sample and, thus, only findings for the full sample are reported here.

DISCUSSION

Findings of this investigation supported the study hypothesis that severity of confusion (as measured by the DelRS-R98) at approximately 1 month after injury provides some prediction of employment outcome at 1 year after injury for patients with TBI. This association was demonstrated with univariable and multivariable logistic regression as well as with correlational analyses. Indeed, severity of confusion at 1 month showed a stronger association with outcome than duration of PTA. This finding provides support for the utility of assessment of severity of confusion at a fixed interval after injury rather than simply assessing duration of PTA. As noted by Tate *et al*, PTA duration depends on the method used to assess PTA status.¹⁷ In some cases, PTA durations may extend considerably beyond 1 month after injury and even beyond the time of discharge from the rehabilitation hospital. In these cases, actual PTA durations

may be difficult or impossible to obtain. The utility of measurement of severity of confusion may be greater for patients with these longer PTA durations.

While severity of confusion was more strongly associated with employment outcome than PTA duration, we also confirmed prior studies reporting that PTA duration is a powerful predictor of outcome after TBI.^{5-7 12-15} In the unadjusted analysis, patients with shorter PTA duration at the 25th percentile were almost three times as likely to be employed at follow-up as were patients at the 75th percentile. Current findings were also consistent with numerous previous investigations in demonstrating that younger age at injury¹²⁻¹⁴ and higher educational level^{7 27} are associated with a more favourable functional outcome after TBI. The proportion of variance in employment outcome accounted for by the current predictive model (34%) is somewhat modest but not surprising given the complexity of predicting a community participation outcome that is influenced by premorbid employment history, family support, disability payments, prevailing economic conditions and a host of other factors.

Severity of confusion showed a strong association with PTA duration. Participants who were more severely confused at 1 month after injury had longer PTA durations than those who were less severely confused at 1 month after injury. While this finding is not surprising, we know of no other demonstration of this result. Our results indicate that disorientation (PTA) is an important aspect of post-traumatic confusion and that there is substantial overlap between the two constructs. However, our findings also demonstrate that post-traumatic confusion is associated with a broad range of symptoms other than disorientation and memory impairment. Many of these symptoms (eg, agitation, sleep disturbance, psychotic-type symptoms) have important implications for patient management. The present results support the utility of measurement of the severity of a wide range of symptoms of confusion rather than just the presence (duration) of disorientation. Again, we know of no other demonstration, in this context, that symptom severity at a given point in time is more predictive of outcome than symptom duration.

While severity of confusion was useful in predicting outcome, symptoms of confusion were not specific to patients who met diagnostic criteria for delirium. Some symptoms such as perceptual disturbance and delusions almost never occurred in non-confused patients; they also only occurred in about 25% of confused patients. Symptoms that were most common in confused patients, such as short term memory impairment, long term memory impairment and visuospatial impairment, were also the most common symptoms for non-confused patients. Symptoms that most differentiated the two groups were motor agitation, thought process abnormalities, disorientation and lability of affect, but even these symptoms had poor specificity for confusion. Given the fact that all patients

were in early recovery from moderate or severe TBI, it is severity of confusion rather than specific symptoms of confusion that is most important to assess.

The current findings should be replicated to demonstrate their generalisability to the general population of patients with TBI who receive inpatient rehabilitation. However, the relatively low rate of loss to follow-up suggests that the current findings likely reflect minimal subject selection. Patients with very severe TBI unable to participate in the study because of being in a minimally conscious or vegetative state were already known to be extremely likely to have poor employment outcomes. The primary limitation of the current investigation is the broad range of injury to evaluation intervals that were coded as "1 month" evaluations. Only approximately 80% of these intervals fell within 2 weeks of the actual 1 month post-injury date. These injury-to-evaluation intervals were likely confounded with injury severity, as patients with milder injuries have shorter intervals because of brief acute and rehabilitation length of stay while patients with more severe injuries have longer intervals as a result of very long acute care length of stay. However, analysis of the subset with intervals within the 2 week window resulted in essentially identical findings.

CONCLUSION

In addition to demographic and traditional injury severity indices, severity of confusion makes a unique contribution to predicting late outcome after TBI. Our findings provide support for the utility of routine assessment of severity of confusion at a fixed time after injury, particularly for those patients who do not show early resolution of PTA. Our finding that severity of confusion was not perfectly associated with PTA duration and our results regarding the wide variety of symptoms shown by confused patients support Stuss *et al's* conceptualisation of post-traumatic confusional state as a more accurate description of the period of early recovery after TBI than the often used post-traumatic amnesia.⁹

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