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ORIGINAL RESEARCH

# Trajectories of Fatigue, Psychological Distress, and Coping Styles After Mild Traumatic Brain Injury: A 6-Month Prospective Cohort Study

Check for updates

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**Abstract**

**Objective:** To analyze fatigue after mild traumatic brain injury (TBI) with latent class growth analysis (LCGA) to determine distinct recovery trajectories and investigate influencing factors, including emotional distress and coping styles.

**Design:** An observational cohort study design with validated questionnaires assessing fatigue, anxiety, depression, posttraumatic stress, and coping at 2 weeks and 3 and 6 months postinjury.

**Setting:** Three level 1 trauma centers.

**Participants:** Patients with mild TBI (N=456).

**Interventions:** Not applicable.

**Main Outcome Measures:** Fatigue was measured with the fatigue severity subscale of the Checklist Individual Strength, including 8 items (sum score, 8-56). Subsequently, 3 clinical categories were created: high (score, 40-56), moderate (score, 26-38), and low (score, 8-25).

**Results:** From the entire mild TBI group, 4 patient clusters with distinct patterns for fatigue, emotional distress, and coping styles were found with LCGA. Clusters 1 and 2 showed favorable recovery from fatigue over time, with low emotional distress and the predominant use of active coping in cluster 1 (30%) and low emotional distress and decreasing passive coping in cluster 2 (25%). Clusters 3 and 4 showed unfavorable recovery, with persistent high fatigue and increasing passive coping together with low emotional distress in cluster 3 (27%) and high emotional distress in cluster 4 (18%). Patients with adverse trajectories were more often women and more often experiencing sleep disturbances and pain.

**Conclusions:** The prognosis for recovery from posttraumatic fatigue is favorable for 55% of mild TBI patients. Patients at risk for chronic fatigue can be signaled in the acute phase postinjury based on the presence of high fatigue, high passive coping, and, for a subgroup of patients, high emotional distress. LCGA proved to be a highly valuable and multipurpose statistical method to map distinct courses of disease-related processes over time.

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Traumatic brain injury (TBI) is a serious public health concern worldwide.[1] Most of these patients (80%-90%) sustain a mild TBI (mTBI).[2] Although the prognosis after mTBI is generally favorable, a common invalidating complaint is feeling excessively fatigued. In the acute phase postinjury, up to 70% of patients with mTBI report excessive fatigue,[3] which can persist for years.[4]

Within the population with mTBI, heterogeneity in symptoms and diversity in recovery patterns are common.[5,6] Given the detrimental consequences of excessive fatigue, it is imperative to early identify subgroups of patients at risk.

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In the existent literature, longitudinal data about fatigue after mTBI is scarce and analyses are often performed on a group-level only, showing a decrease of fatigue up to 3 months postinjury, followed by a relatively stable level of remaining fatigue over time.[3,6] The present study adds value to the existing literature because it is the largest follow-up study investigating fatigue after mTBI, making clinically relevant distinctions between subgroups of patients showing distinct fatigue recovery patterns using latent class growth analysis (LCGA).[7] LCGA is a statistical method allowing identification of unobserved subpopulations ("clusters") that show specific, distinct patterns of longitudinal change ("trajectories"). The merit of this approach has already been demonstrated in research investigating neurodegenerative processes, providing information about subgroups of patients showing either slow or rapid dementia progression.[8] With LCGA, patients can be signaled early based on levels of relevant symptoms at onset and subgroup characteristics.

Including other variables that strongly influence fatigue in the LCGA is critical to the interpretation of the results.[6] Feeling depressed may exacerbate fatigue, and feeling persistently fatigued may strengthen depressive feelings. Furthermore, patients may develop anxiety and posttraumatic stress, resulting in sleeping difficulties.[9,10] Additionally, coping style, the way one deals with stressful situations, has also been related to fatigue levels.[6] Coping style is generally divided into active coping (an external problem-solving approach) and passive coping (a more internal emotion-focused approach). Having a passive coping style (eg, worrying) has been related to elevated levels of fatigue.[7]

This is the first study to examine distinct trajectories of fatigue, emotional distress, and coping styles after mTBI in a large cohort study using LCGA. Furthermore, subgroup characteristics (demographics, injury severity, bodily injury, sleep disturbances) were examined.

# Methods

## Design and setting

Present data originated from a larger prospective longitudinal study (UPFRONT study).[11] Patients were admitted at 3 level 1 trauma centers in the Netherlands. The Glasgow Coma Scale (GCS) score and posttraumatic amnesia were determined during a neurologic examination at the emergency department (ED). Furthermore, patients completed questionnaires at 2 weeks and 3 and 6 months postinjury. Data obtainment occurred in compliance with ethical regulations of the University Medical Center Groningen, following the Declaration of Helsinki, and patients signed informed consent.

***List of abbreviations:***

| | |
|---|---|
| **BIC** | **Bayesian information criterion** |
| **CBT** | **cognitive behavioral therapy** |
| **ED** | **emergency department** |
| **GCS** | **Glasgow coma scale** |
| **LCGA** | **latent class growth analysis** |
| **mTBI** | **mild traumatic brain injury** |
| **TBI** | **traumatic brain injury** |
| **YOE** | **years of education** |

## Participants

In the period between January 25, 2013 and January 6, 2015, patients with mTBI, admitted to the EDs of participating centers were approached for participation in the study. mTBI was defined by a GCS score of 13-15, posttraumatic amnesia duration of ≤24 hours, or loss of consciousness of <30 minutes.[11,12] The exclusion criteria were age <16 years, alcohol or drug abuse, major psychiatric or neurologic disorders, no permanent home address, and insufficient command of the Dutch language.

## Measures included in LCGA

Three time intervals (2wk, 3 and 6mo postinjury) were included in LCGA. To allow for a direct clinically relevant interpretation of the LCGA results, each dependent variable was categorized into clinically relevant categories: low, moderate, and high. This was done based on default norm scores if available, and available literature otherwise.

### Fatigue

Fatigue was measured with the fatigue severity subscale of the Checklist Individual Strength,[13] including 8 items measuring fatigue symptoms over the past 2 weeks, with scores classified as high (40-56), moderate (26-39), and low (8-25).[14]

### Anxiety and depression

Anxiety and depression were assessed using the Hospital Anxiety and Depression Scale,[15] including 14 items measuring both constructs separately, with scores being classified as high (11-21), moderate (8-10), and low (0-7).

### Posttraumatic stress

Posttraumatic stress was measured using the Impact of Event Scale,[16] including 15 items with scores being classified as high (30-75), moderate (19-30), and low (0-18).

### Coping

Coping style was assessed with the Utrecht Coping List,[17] a 47-item questionnaire. Subscales of the Utrecht Coping List measuring active and passive coping were included, each consisting of 7 items (7-28). Scores were, relative to a norm group based on sex, categorized as very low (1), low (2), average (3), high (4), and very high (5). Subsequently, for the present study, these categories were classified as high (4-5), moderate (3), and low (1-2).

## Demographic, clinical, and outcome characteristics

### Demographics

Age at injury was categorized as <29 years, 30-39 years, 40-49 years, 50-59 years, 60-69 years, and ≥70 years.

Education level was classified based on years of education (YOE) according to the Dutch 7-point scale (1 indicates primary school [<6 YOE], 2 indicates finished primary school [6 YOE], 3 indicates did not finish secondary school [7-8 YOE], 4 indicates finished secondary school [9 YOE], 5 indicates finished secondary school [10-11 YOE], 6 indicates finished secondary school [12-16 YOE], and 7 indicates university degree [>16 YOE]). This was subsequently classified as high (6-7), moderate (4-5), and low (1-3).

### Injury severity

Injury severity was assessed using the GCS score[18] and was categorized based on a GCS score of 15, 14, and 13.

### Pain

Pain was assessed based on 3 questions (headache, neck, and arm pain) from the Head Injury Symptom Checklist[19] answered with absent (0), sometimes (1), or often (2) and categorized as absent or sometimes (0 or 1 on all questions) and often (2 on ≥1 questions).

### Fractures

Fractures to ribs and/or extremities were noted and classified as present and absent.

### Sleep

Sleep disturbances at 6 months were assessed based on 3 questions (Head Injury Symptom Checklist)[19] considering excessive need of sleep, problems falling asleep, and problems sleeping through the night, answered with absent (0), sometimes (1), or often (2). Patients also reported retrospectively how their sleeping characteristics had been before the injury.

## Statistical analysis

Data were analyzed using SPSS, version 25.0,[a] and Latent GOLD, version 5.1.[20,b] Patients with missing data for fatigue were excluded. To verify whether patients in this study were representative of the entire group of patients with mTBI included in the UPFRONT study,[11] we made comparisons for demographic and clinical characteristics using *t* tests, Mann-Whitney *U* tests, and chi-square tests, with Bonferroni-Holm correction for multiple comparisons. Furthermore, pairwise correlations between the dependent variables were calculated at 2 weeks, 3 months, and 6 months postinjury.

LCGA was performed to identify distinct clusters of patients that showed a similar pattern of longitudinal change across the domains of fatigue, emotional distress, and coping styles.[7] In this analysis, all 6 dependent variables (fatigue, anxiety, and depression measured at 2 weeks, 3 months, and 6 months postinjury and posttraumatic stress, active coping, and passive coping measured at 2 weeks and 6 months postinjury) were simultaneously modeled. Specifically, in the LCGA, the trajectory of each dependent variable per cluster was modeled with an adjacent-category logit model, using a linear function of time (coded as 0, 1, and 2), with the intercept referring to the measurement at 2 weeks and the slope referring to the general degree of increase or decrease across time. LCGA models with 1 up to 9 clusters were estimated. From these 9 models, we selected the model with the lowest Bayesian Information Criterion (BIC) and proper interpretability. The BIC, a statistical index of model fit, is a commonly used index for latent class models that penalizes the complexity of the model.[21] The selected LCGA model thus has a certain number of patient clusters, with each cluster representing a specific trajectory with regard to each of the 6 dependent variables.

Characteristics of patients following each of the identified trajectories were subsequently assessed by relating demographic and clinical characteristics (age, education, sex, GCS scores, pain, fractures, and 3 pre- and postinjury sleep characteristics) of the patients with mTBI to the identified clusters. This was done per characteristic using the characteristic as a predictor for cluster membership, using a multinomial logistic regression analysis with adjustment for classification errors[22] and with Bonferroni-Holm correction for multiple comparisons (correcting for the 7 demographic and clinical characteristics). For all analyses, the nominal significance level was set at .05 2-sided.

# Results

## Participants

We included 456 patients with mTBI who completed assessments at 2 weeks (mean, 18±8d), 3 months (mean, 88±10d), and 6 months (mean, 183±24d) postinjury. The mean age was 49±19 years (range, 16-92y), the mean education level score was 5.3±1.3 (range, 3-7), and 58% were men. The mean GCS score was 14.6±0.6 (range, 13-15). This group of patients was comparable to the total patient group included in the UPFRONT study (n=1169; the fatigue questionnaire was not completed by 409 participants at 2 weeks, 197 participants at 3 months, and 107 participants at 6 months), on sex, education level, and GCS score, but were somewhat older (the mean age of the total group was 41±20y; $t = -6.67$; $P<.001$).

## Correlations between fatigue, emotional distress, and passive coping

Fatigue was significantly strongly correlated with anxiety and depression and significantly moderately correlated with posttraumatic stress and passive coping (supplemental table S1, available online only at http://archives-pmr.org/).

## Distinct clusters

Out of the 9 LCGA models, the model with 4 clusters was selected, because it had the lowest BIC and was interpretable. In this model, all clusters differed significantly from each other at 2 weeks (ie, intercept) on fatigue, emotional variables, and coping styles, whereas the general trend (ie, slope) only differed significantly between clusters for fatigue and passive coping. For all patient clusters, the general trend changed significantly over time for fatigue and passive coping. For each of the 4 clusters, the trajectories for fatigue, anxiety, depression, posttraumatic stress, and passive coping are presented in figures 1-4. The percentages indicate for each patient belonging to the cluster involved the probability of responding in the low, moderate, or high category, respectively, for each of the dependent variables. Results show that active coping did not differ significantly across the clusters and across time and is reported in text only.

### Cluster 1: complete recovery from fatigue in combination with active coping

The first cluster represents 30% (n=137) of the patients with mTBI (see fig 1). At 2 weeks postinjury, 8% of patients reported high fatigue and 31% reported moderate fatigue. This improved substantially over time, with 0% of the patients reporting high levels of fatigue and 7% reporting moderate fatigue at 6 months postinjury. Additionally, anxiety and depression were absent, and only 2% experienced symptoms of posttraumatic stress. Furthermore, 0% used passive coping, and 31% used active coping.

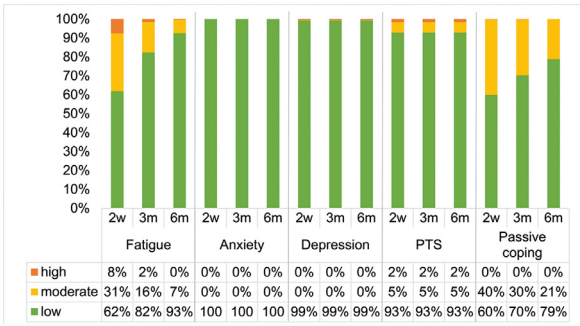


**Fig 1** Cluster 1: complete recovery from fatigue in combination with active coping, comprising 30% (n=137) of the patients with mTBI. Percentages reflect the probabilities of patients to belong in the low, moderate, or high category for fatigue, emotional distress, and passive coping. PTS, posttraumatic stress.

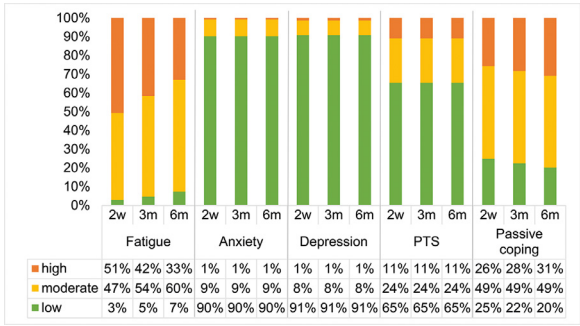


**Fig 3** Cluster 3: persistent fatigue without emotional distress, comprising 27% (n=123) of the patients with mTBI. Percentages reflect the probabilities of patients to belong in the low, moderate, or high category for fatigue, emotional distress, and passive coping. PTS, posttraumatic stress.

### Cluster 2: decreasing fatigue and decreasing passive coping

The second cluster represents 25% (n=114) of the patients with mTBI (see fig 2). At 2 weeks postinjury, 19% of patients reported high fatigue and 41% reported moderate fatigue. The initially experienced fatigue decreased profoundly over time, with 1% of the patients reporting high levels of fatigue and 12% reporting moderate fatigue at 6 months postinjury. Additionally, the presence of symptoms of anxiety (1%), depression (1%), and posttraumatic stress (14%) was limited. Furthermore, decreasing the use of passive coping (39% to 26%) was found, and 23% used active coping.

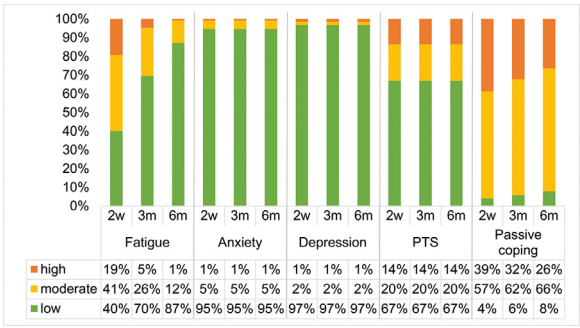


**Fig 2** Cluster 2: decreasing fatigue and decreasing passive coping, comprising 25% (n=114) of the patients with mTBI. Percentages reflect the probabilities of patients to belong in the low, moderate or high category for fatigue, emotional distress, and passive coping. PTS, posttraumatic stress.

### Cluster 3: persistent fatigue without emotional distress

This cluster represents 27% (n=123) of the patients with mTBI (see fig 3). At 2 weeks postinjury, 51% of the patients reported high fatigue and 47% reported moderate fatigue. The fatigue complaints were persistent over time, with 33% of the patients reporting high levels of fatigue and 60% reporting moderate fatigue at 6 months postinjury. Additionally, the presence of symptoms of anxiety (1%), depression (1%), and posttraumatic stress (11%) was low. Furthermore, a trend toward increasing use of passive coping (26% to 31%) was found, and 22% used active coping.

### Cluster 4: persistent fatigue with emotional distress

This cluster represents 18% (n=82) of the patients with mTBI (see fig 4). At 2 weeks postinjury, 74% of patients reported high fatigue and 23% reported moderate fatigue. The fatigue complaints persisted over time, with 55% of the patients reporting high levels of fatigue and 36% reporting moderate fatigue at 6 months postinjury. Additionally, the presence and persistence of symptoms of anxiety (40%), depression (29%), and posttraumatic stress (58%) were evident. Furthermore, a high and significantly increasing use of passive coping (69% to 86%) was found, and 17% used active coping.

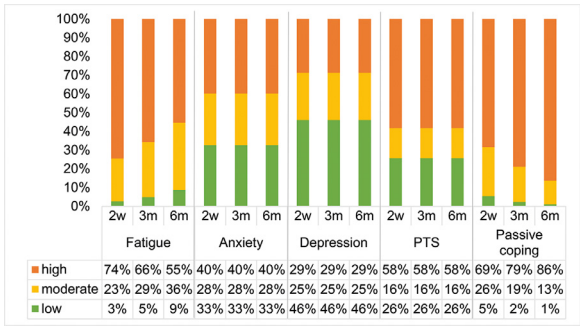


**Fig 4** Cluster 4: persistent fatigue with emotional distress, comprising 18% (n=82) of the patients with mTBI. Percentages reflect the probabilities of patients to belong in the low, moderate, or high category for fatigue, emotional distress, and passive coping. PTS, posttraumatic stress.

## Demographic and clinical characteristics

Across all patient clusters, significant differences were found for sex, education level, outcome, and pain (table 1). Clusters 3 and 4 consisted of significantly more women; individuals in these clusters experienced pain more often than those in cluster 1. Moreover, patients in cluster 4 had a significantly lower education level compared with clusters 2 and 3. No significant differences between clusters were found for age, injury severity, and fractures.

**Table 1** Demographic and clinical characteristics

| | Clusters | | | | Comparisons | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Variable | 1 30% | 2 25% | 3 27% | 4 18% | Clusters | | | Wald(0) | *df* | *P* Value |
| **Age, %** | | | | | | | | | | |
| ≤29 y | 20 | 28 | 21 | 22 | Across all clusters | | | 2.74 | 3 | .430 |
| 30-49 y | 23 | 25 | 23 | 23 | 1 | vs | 2 | 2.52 | 1 | .110 |
| 50-59 y | 19 | 18 | 19 | 19 | 1 | vs | 3 | 0.10 | 1 | .750 |
| 60-69 y | 22 | 18 | 21 | 21 | 1 | vs | 4 | 0.21 | 1 | .650 |
| ≥70 y | 16 | 11 | 15 | 15 | 2 | vs | 3 | 0.03 | 1 | .870 |
| | | | | | 2 | vs | 4 | 1.27 | 1 | .260 |
| | | | | | 3 | vs | 4 | 0.03 | 1 | .870 |
| **Sex, %** | | | | | | | | | | |
| Women | 27 | 42 | 48 | 58 | Across all clusters | | | 18.80 | 3 | <.001* |
| Men | 73 | 59 | 52 | 42 | 1 | vs | 2 | 3.79 | 1 | .052 |
| | | | | | 1 | vs | 3 | 9.07 | 1 | .003* |
| | | | | | 1 | vs | 4 | 16.92 | 1 | <.001* |
| | | | | | 2 | vs | 3 | 0.62 | 1 | .430 |
| | | | | | 2 | vs | 4 | 4.11 | 1 | .043 |
| | | | | | 3 | vs | 4 | 1.66 | 1 | .200 |
| **Education level, %** | | | | | | | | | | |
| Low | 6 | 3 | 4 | 12 | Across all clusters | | | 14.78 | 3 | .002* |
| Medium | 46 | 36 | 40 | 54 | 1 | vs | 2 | 3.24 | 1 | .072 |
| High | 47 | 61 | 56 | 34 | 1 | vs | 3 | 1.80 | 1 | .180 |
| | | | | | 1 | vs | 4 | 4.30 | 1 | .038 |
| | | | | | 2 | vs | 3 | 0.34 | 1 | .560 |
| | | | | | 2 | vs | 4 | 12.20 | 1 | .000* |
| | | | | | 3 | vs | 4 | 8.67 | 1 | .003* |
| **Injury severity, %** | | | | | | | | | | |
| 13 | 4 | 5 | 6 | 7 | Across all clusters | | | 3.07 | 3 | .380 |
| 14 | 26 | 28 | 31 | 33 | 1 | vs | 2 | 0.04 | 1 | .840 |
| 15 | 69 | 68 | 62 | 60 | 1 | vs | 3 | 1.24 | 1 | .270 |
| | | | | | 1 | vs | 4 | 2.19 | 1 | .140 |
| | | | | | 2 | vs | 3 | 0.61 | 1 | .430 |
| | | | | | 2 | vs | 4 | 1.35 | 1 | .250 |
| | | | | | 3 | vs | 4 | 0.17 | 1 | .680 |
| **Outcome, %** | | | | | | | | | | |
| ≤Upper moderate disability | 10 | 13 | 52 | 55 | Across all clusters | | | 80.70 | 3 | <.001* |
| Lower good recovery | 11 | 13 | 17 | 16 | 1 | vs | 2 | 0.51 | 1 | .480 |
| Upper good recovery | 79 | 74 | 32 | 28 | 1 | vs | 3 | 41.72 | 1 | <.001* |
| | | | | | 1 | vs | 4 | 43.15 | 1 | <.001* |
| | | | | | 2 | vs | 3 | 31.01 | 1 | <.001* |
| | | | | | 2 | vs | 4 | 33.69 | 1 | <.001* |
| | | | | | 3 | vs | 4 | 0.22 | 1 | .640 |
| **Pain, %** | | | | | | | | | | |
| Absent or sometimes | 95 | 87 | 65 | 42 | Across all clusters | | | 56.20 | 3 | <.001* |
| Often | 5 | 13 | 35 | 58 | 1 | vs | 2 | 2.89 | 1 | .089 |
| | | | | | 1 | vs | 3 | 19.17 | 1 | <.001* |
| | | | | | 1 | vs | 4 | 36.01 | 1 | <.001* |
| | | | | | 2 | vs | 3 | 9.40 | 1 | .002* |
| | | | | | 2 | vs | 4 | 27.94 | 1 | <.001* |
| | | | | | 3 | vs | 4 | 7.91 | 1 | .005* |
| **Fractures, %** | | | | | | | | | | |
| Absent | 86 | 86 | 78 | 85 | Across all clusters | | | 3.32 | 3 | .340 |
| Present | 14 | 14 | 22 | 15 | 1 | vs | 2 | 0.01 | 1 | .930 |
| | | | | | 1 | vs | 3 | 2.55 | 1 | .110 |
| | | | | | 1 | vs | 4 | 0.04 | 1 | .850 |
| | | | | | 2 | vs | 3 | 1.72 | 1 | .190 |
| | | | | | 2 | vs | 4 | 0.01 | 1 | .930 |
| | | | | | 3 | vs | 4 | 1.44 | 1 | .230 |

Comparisons were made across all clusters and between independent clusters.
* Significant after Bonferroni—Holm correction.

### Sleep characteristics

Across all clusters, significant differences were found for sleep disturbances (supplemental tables S2 and S3, available online only at http://archives-pmr.org/). At a preinjury level, patients in clusters 3 and 4 experienced more sleep disturbances compared with those in cluster 1. Furthermore, clusters 3 and 4 showed evident increases in sleep disturbances from pre- to postinjury.

## Discussion

This is the first study investigating fatigue after mTBI in a large longitudinal cohort study using LCGA to identify different subgroups of patients (clusters) that show distinct trajectories of fatigue, emotional distress, and coping styles over time. We identified 4 distinct patient clusters. The prognosis for recovery from posttraumatic fatigue was favorable for 2 clusters, comprising 55% of the patients. The other 2 clusters, comprising 45% of the patients, had an unfavorable prognosis and had in common that levels of fatigue were already high in the acute phase postinjury and remained high over time. Patients at risk for chronic high fatigue can be signaled early in the acute phase postinjury based on the presence of high fatigue, high passive coping and, for one cluster, high anxiety, depression, and posttraumatic stress. Increasing levels of passive coping, often considered an unconstructive way of dealing with problems,[23] were especially found to distinguish unfavorable from favorable clusters. Furthermore, patients from the unfavorable clusters were more often women and were more likely to experience sleep disturbances and pain.

Two distinct favorable clusters were identified, both showing recovery from fatigue over time with patients experiencing virtually no emotional distress during their recovery. In cluster 1 (complete recovery from fatigue in combination with active coping), fatigue complaints were initially low and completely resolved by 6 months. These patients predominantly had an active coping style, generally defined as an effective way of dealing with stressful situations.[23] Cluster 2 (decreasing fatigue and decreasing passive coping) showed initially higher fatigue scores but these diminished over time. Interestingly, patients initially reported higher passive coping levels but these decreased over time.

There was a crucial and remarkable difference between both unfavorable clusters: cluster 3 (persistent fatigue without emotional distress) was characterized by almost no indication for the presence of emotional distress, whereas cluster 4 (persistent fatigue with emotional distress) reported high levels of anxiety, depression, and posttraumatic stress. A second difference between the unfavorable clusters concerned education level, with patients in cluster 3 having a higher education level and patients in cluster 4 having a lower education level.

Based on the profile of the different clusters, it could be tentatively concluded that recovery from excessive fatigue will be more favorable when patients have an active coping style combined with little or no passive coping and emotional distress. Previous research indicated that coping strategy use in patients with TBI may be effectively modified through cognitive behavioral therapy (CBT).[24,25] With CBT, patients with a passive coping style can be challenged to investigate links between beliefs, thoughts, and behavior. Potential misinterpretations about fatigue can be replaced by thoughts that are based on more adequate beliefs.[24,26] A combination of CBT and graded exercise therapy has been shown to improve fatigue levels in chronic fatigue patients, primarily through the reduction of "fear-avoidance behaviors."[26]

LCGA proved to be a powerful method to identify distinct patient clusters that show different trajectories of fatigue, emotional distress, and coping styles over time. Clinically relevant characteristics with great prognostic value can be determined as early as 2 weeks after injury, providing clues for the expected outcome and early intervention. This study proves LCGA to be a highly valuable and broadly applicable statistical method for studying changes over time in disease-related processes.

### Study limitations

The findings in this study must be seen in the light of some limitations. Patients in this study were likely slightly older than the population with mTBI at large, which should be considered with regard to the generalizability of our results. Furthermore, information about preinjury patient characteristics (fatigue, emotional distress, coping styles) was not available. Hence, it is not possible to disentangle the influence of injury-related consequences and premorbid vulnerabilities on postinjury fatigue. Another limitation is that our measure for fatigue did not allow us to discern mental from physical fatigue. Possibly, patients with physical injuries mainly reported physical fatigue. However, when comparing fractures between the distinct patient clusters, no significant difference was found. Lastly, it is important to bear in mind that, given the observational design, the present study does not allow for any conclusion on the directionality of the relationships between variables (eg, fatigue and emotional distress).

## Conclusions

In conclusion, the findings of this study offer clues for the early identification of patients at risk for an adverse course of persistent and excessive fatigue. Becoming chronically fatigued can have detrimental consequences for the overall outcome and reintegration into society. A specific subgroup of patients with high levels of fatigue and high passive coping in the acute phase after injury seems vulnerable to adverse fatigue recovery patterns. Because having an adequate coping style and having less emotional distress was found in combination with a more favorable recovery from fatigue, treatments (eg, CBT and graded exercise therapy) that decrease passive coping and emotional distress should be studied in patients with high fatigue to determine whether they decrease adverse outcomes. Noticeably, attention must be paid to the relief of pain and the presence of sleep disturbances.

## Suppliers

a. SPSS, version 25.0; IBM Inc.
b. Latent GOLD, version 5.1; Statistical Innovations.

## Keywords

Brain concussion; Fatigue; Psychological distress; Rehabilitation; Traumatic brain injury

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**Supplementary Table 1** Correlations between fatigue, emotional distress and passive coping for the entire TBI sample

| | | | | | |
|---|---|---|---|---|---|
| **2 weeks** | | | | | |
| | Fatigue | Anxiety | Depression | PTS | Passive coping |
| Fatigue | | .527** | .606** | .373** | .290** |
| Anxiety | .527** | | .671** | .620** | .547** |
| Depression | .606** | .671** | | .427** | .390** |
| PTS | .373** | .620** | .427** | | .415** |
| Passive coping | .290** | .547** | .390** | .415** | |
| **3 months** | | | | | |
| | Fatigue | Anxiety | Depression | | |
| Fatigue | | .645** | .699** | | |
| Anxiety | .645** | | .711** | | |
| Depression | .699** | .711** | | | |
| **6 months** | | | | | |
| | Fatigue | Anxiety | Depression | PTS | Passive coping |
| Fatigue | | .590** | .684** | .473** | .495** |
| Anxiety | .590** | | .686** | .603** | .625** |
| Depression | .684** | .686** | | .599** | .549** |
| PTS | .473** | .603** | .599** | | .479** |
| Passive coping | .495** | .625** | .549** | .479** | |

PTS=posttraumatic stress
*$p<.05$,
** $p<.01$, *** $p<.001$

**Supplementary Table 2** Sleep characteristics

| | Clusters | | | | Comparisons | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | | | | | | |
| | 30% | 25% | 27% | 18% | Clusters | | | Wald(0) | df | *p* |
| **Pre-injury "Excessive need of sleep"** | | | | | | | | | | |
| No | 61% | 44% | 39% | 44% | across all clusters | | | 34.25 | 3 | .000* |
| Sometimes | 33% | 42% | 43% | 41% | 1 | vs. | 2 | 59.95 | 1 | .014 |
| Often | 6% | 13% | 18% | 15% | 1 | vs. | 3 | 260.16 | 1 | .000* |
| | | | | | 1 | vs. | 4 | 199.20 | 1 | .000* |
| | | | | | 2 | vs. | 3 | 80.35 | 1 | .005* |
| | | | | | 2 | vs. | 4 | 6.37 | 1 | .012 |
| | | | | | 3 | vs. | 4 | 0.01 | 1 | .920 |
| **Pre-injury "Problems falling asleep"** | | | | | | | | | | |
| No | 84% | 75% | 72% | 54% | across all clusters | | | 30.72 | 3 | .000* |
| Sometimes | 14% | 21% | 23% | 33% | 1 | vs. | 2 | 30.91 | 1 | .079 |
| Often | 2% | 4% | 5% | 13% | 1 | vs. | 3 | 8.29 | 1 | .004* |
| | | | | | 1 | vs. | 4 | 281.30 | 1 | .000* |
| | | | | | 2 | vs. | 3 | 0.99 | 1 | .320 |
| | | | | | 2 | vs. | 4 | 131.87 | 1 | .000* |
| | | | | | 3 | vs. | 4 | 85.40 | 1 | .004* |
| **Pre-injury "Problems sleeping through the night"** | | | | | | | | | | |
| No | 80% | 58% | 65% | 51% | across all clusters | | | 28.81 | 3 | .000* |
| Sometimes | 18% | 32% | 29% | 36% | 1 | vs. | 2 | 124.21 | 1 | .000* |
| Often | 2% | 10% | 6% | 13% | 1 | vs. | 3 | 107.32 | 1 | .001* |
| | | | | | 1 | vs. | 4 | 280.81 | 1 | .000* |
| | | | | | 2 | vs. | 3 | 0.04 | 1 | .840 |
| | | | | | 2 | vs. | 4 | 40.03 | 1 | .045 |
| | | | | | 3 | vs. | 4 | 40.12 | 1 | .045 |

Comparisons were made across all clusters and between independent clusters.
* significant after Bonferroni–Holm correction.

**Supplementary Table 3** Comparisons of pre- and post-injury sleep disturbances

| | Clusters | | | | | | | Comparisons | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | Clusters | | | Wald(0) | Df | *P* |
| | 30% | 25% | 27% | 18% | | | | | | |
| **Changes in "Excessive need of sleep"** | | | | | | | | | | |
| Evident increase | 2% | 1% | 13% | 17% | across all clusters | | | 55.16 | 3 | 0.000* |
| Slight increase | 18% | 15% | 36% | 39% | 1 | vs. | 2 | 0.04 | 1 | 0.840 |
| Similar amount | 78% | 81% | 51% | 44% | 1 | vs. | 3 | 34.19 | 1 | 0.000* |
| Decrease | 2% | 3% | 1% | 0% | 1 | vs. | 4 | 37.70 | 1 | 0.000* |
| | | | | | 2 | vs. | 3 | 23.35 | 1 | 0.000* |
| | | | | | 2 | vs. | 4 | 28.22 | 1 | 0.000* |
| | | | | | 3 | vs. | 4 | 0.51 | 1 | 0.480 |
| **Changes in "Problems falling asleep"** | | | | | | | | | | |
| Evident increase | 1% | 1% | 6% | 8% | across all clusters | | | 25.45 | 3 | 0.000* |
| Slight increase | 10% | 11% | 23% | 26% | 1 | vs. | 2 | 0.46 | 1 | 0.500 |
| Similar amount | 88% | 85% | 71% | 65% | 1 | vs. | 3 | 13.11 | 1 | 0.000* |
| Decrease | 1% | 2% | 1% | 1% | 1 | vs. | 4 | 19.84 | 1 | 0.000* |
| Evident decrease | 0% | 0% | 0% | 0% | 2 | vs. | 3 | 10.11 | 1 | 0.002* |
| | | | | | 2 | vs. | 4 | 15.94 | 1 | 0.000* |
| | | | | | 3 | vs. | 4 | 2.01 | 1 | 0.160 |
| **Changes in "Problems sleeping through the night"** | | | | | | | | | | |
| Evident increase | 1% | 1% | 10% | 11% | across all clusters | | | 35.05 | 3 | 0.000* |
| Slight increase | 9% | 12% | 27% | 30% | 1 | vs. | 2 | 1.12 | 1 | 0.290 |
| Similar amount | 89% | 85% | 63% | 59% | 1 | vs. | 3 | 22.42 | 1 | 0.000* |
| Decrease | 1% | 2% | 0% | 0% | 1 | vs. | 4 | 28.18 | 1 | 0.000* |
| | | | | | 2 | vs. | 3 | 10.59 | 1 | 0.001* |
| | | | | | 2 | vs. | 4 | 15.40 | 1 | 0.000* |
| | | | | | 3 | vs. | 4 | 1.12 | 1 | 0.290 |

Comparisons were made across all clusters and between independent clusters.
* significant after Bonferroni—Holm correction.