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Decline in cognitive function due to diffuse axonal injury does not necessarily imply a corresponding decline in ability to perform activities.

Abstract

Purpose

The study explored the direction of change (decline vs. improvement) after diffuse axonal injury (DAI) in the domains of the ICF: body structure, body function, and activity.

Methods

Thirteen patients with DAI were assessed by using diffusion tensor imaging (DTI) to measure body structure, the Barrow Neurological Institute Screen for Higher Cerebral Functions (BNIS) to measure body function, and the Assessment of Motor and Process Skills (AMPS) to measure activity. The DTI, BNIS, and AMPS were applied at the acute phase (A1), and at 6 and 12 months post-injury (A2 and A3). Visual and statistical analyses were conducted to explore time-dependent changes in the ICF domains.

Results

Improvements were observed for most patients in all ICF domains from injury until 6 months. Thereafter, the results diverged, with half of the subjects showing a decline in DTI and BNIS scores between A2–A3, and all but one of the patients exhibiting identical or better A2–A3 AMPS process skill scores.

Conclusions

From 6 to 12 months post-injury, some patients underwent an ongoing degenerative process, causing a decline in cognitive function. The same decline was not observed in the activity measure, which might be explained by the use of compensatory strategies.

Introduction

Traumatic brain injury (TBI) exhibits a complex and heterogeneous pathology, often producing long-lasting cognitive and behavioral impairments and disability [1]. Diffuse axonal injury (DAI) is among the most common neuropathological consequences of TBI and accompanies all injury categories and severities [2]. DAI probably contributes to the majority of persistent cognitive difficulties experienced by ~7–33% of individuals with mild TBI, although the brains of these individuals appear normal on conventional neuroimaging scans [3].

TBI encompasses focal lesions caused by impact, as well as diffuse damage to white matter connections. The latter are caused by acceleration-deceleration events in the brain and lead to the disconnection of affected brain regions [4]. Conventional imaging techniques, such as those afforded by computed tomography (CT) and standard magnetic resonance imaging (MRI), frequently underestimate the extent of white matter damage. Therefore, magnetic resonance diffusion tensor imaging (MR-DTI) is now commonly used to visualize DAI [5, 6]. DTI is a useful and objective means to evaluate the relationship between initial TBI and subsequent cognitive deficits, and to predict the degree of anticipated recovery [7].

The natural progression of cognitive and functional recovery has been widely studied and generally consists of a rapid recovery phase during the first few months after injury, followed by a plateau at 6–18 months post-injury [8]. Recent evidence suggests that TBI may provoke long-term neurodegenerative consequences, in agreement with reports of cognitive decline well after injury [8, 9]. Thus, DAI may be a primary mechanism of post-traumatic neuronal atrophy, as well as a bio-marker of cognitive outcome after brain trauma [10, 11]. However, conflicting results were documented by Sidaros et al. [12], who reported remarkable clinical improvements despite progressive atrophy. Similarly, Moen et al. [13] observed no association between global outcomes and neuroimaging data, implying that factors other than neuronal integrity might influence cognitive status.

Toglia and colleagues [14] formulated a hypothesis that may explain these divergent results. The investigators proposed that all individuals use cognitive strategies, either consciously or automatically, to acquire new skills and/or to cope with a demanding activity or problem. Hence, TBI patients may over time develop and use new strategies to compensate for their loss in cognitive function [14]. The hypothesis of Toglia et al. requires an innovative approach in order to confirm or dispute it.

A useful perspective in this research could be the WHO classification, International Classification of Functioning, Disability, and Health (ICF), with its different domains 1) body structure, 2) body function, and 3) activity and participation, that provide a tool to explore how different aspects contribute to functioning and health [15]. As DAI is a neuropathological consequence of TBI a substantial part of the existing literature describes it in terms of body structure (atrophy, white matter damage) resulting in a changed body function (cognitive function). However, to learn about "real life" we need to study activity and participation dimensions of living with a TBI. The ICF takes a neutral stand with regard to etiology, such that research can more freely explore the causal factors, influence from environment and personal factors, and relationships between different aspects of the ICF. This could mean that the use of the ICF in research may provide a wider perspective on the rehabilitation after TBI.

Accordingly, the aim of the present pilot study was to explore the initial status of a cohort of TBI patients and the direction of change (decline vs. improvement) after suspected DAI in the three separate domains of the International Classification of Functioning, Disability, and Health (ICF): 1) body structure, 2) body function, and 3) activity and participation.

Methods

Study overview

The current study included all patients (age, 18–65 years; n = 22) admitted to Sahlgrenska University Hospital (Gothenburg, Sweden) from June 2006 through to September 2009 who had sustained TBI and, according to clinical and radiological assessment, suffered from suspected DAI (Table 1). Initially, the patients presented with affected consciousness and/or focal neurological symptoms without an obvious alternative explanation on the initial CT brain scan. Patients were subsequently scanned by using MR-DTI within 11 days of injury to record the extent of acute DAI (assessment A1), and again at 6 and 12 months post-injury (assessments A2 and A3, respectively) to record the extent of recovery or deterioration.

Neuropsychological status was assessed by using the Barrow Neurological Institute Screen for Higher Cerebral Functions (BNIS) within 2 weeks of injury (i.e., during the acute phase, A1), and again at 6 and 12 months post-injury. If the patient was not testable, screening was deferred until the Glasgow Coma Scale (GCS) score was >14, or above the cut-off level of the cognitive pre-

screening BNIS score. The BNIS was administered to all patients by a licensed neuropsychologist.

Activities of daily living (ADL) were assessed by using the Assessment of Motor and Process Skills (AMPS). The AMPS is an instrument for the observation and evaluation of occupational performance in two domains of ADL: motor skills (skills involving fine or gross motion or movement) and process skills (skills used to manage and modify actions in the completion of daily tasks) [16]. AMPS assessment was performed at the same time points chosen for BNIS assessment (A1, A2, and A3). The AMPS was administered to all patients by a clinical occupational therapist, trained and certified in the implementation of the test.

The time points of 6 and 12 months were selected since our earlier report [9] suggested an unexpected decline in cognitive function for some patients during the 6–12 month post-injury period. Thus, this interval was particularly interesting for the exploration of BNIS- and AMPS-assessed activity. The BNIS and AMPS instruments are discussed in greater detail below. Work/employment status was also recorded at the 12 month post-injury follow-up.

From the 22 patients initially included in the study, one patient died shortly after arrival at the hospital, and another was lost to follow-up. Accordingly, only 20 patients remained in the study. However, this analysis was limited by missing BNIS and/or AMPS data at some time points (typically, A1). At this time point, a number of patients had not yet recovered sufficiently to be testable. Given that the present investigation focused on the exploration of serial changes in the ability of DAI patients to perform activities after injury, patients without complete AMPS assessments at 6 and 12 months were excluded from the final analysis.

In cases of missing data at baseline due to low-functioning patients, TBI outcomes were interpreted as "improvement" if the AMPS assessment could be performed at 6 months. This denoted that the final patient cohort consisted of 13 individuals (Table 1), including seven men and six women. The mean age of the patients was 34 years (standard deviation (SD) = 16), and the median age was 25 years (range = 19–62). In all cases, the causes of brain trauma were falls (n = 4) and traffic accidents (n = 9).

ICF-based assessments

Assessment of ICF-classified body structure (integrity of white matter axon tracts)

MR-DTI was utilized to assess structural injury of the corpus callosum of the brain, as previously described by our group to analyze the DTI properties of the corpus callosum [11]. DTI measures

water diffusion, its directionality in three dimensions, and diffusion anisotropy, which together allow for an indirect evaluation of the integrity of the white matter tracts. Fractional anisotropy (FA) and diffusivity, expressed as trace or mean diffusivity, are related to structural brain changes and clinical outcomes. FA values range from 0 to 1, with lower values potentially representing a pathologic process. On the other hand, higher trace values might signify organic damage, and an increase in trace values between assessments could signify an ongoing neurodegenerative process.

Assessment of ICF-classified body function (cognition)

The BNIS was previously used to measure cognitive function [17] and has been validated for this purpose in Sweden [18, 19]. The initial BNIS pre-screen assesses whether the patient is testable or not according to consciousness/alertness, basic communicative ability, and active participation in the evaluation. The BNIS entails seven subscales and generates a total score, which was used in the present study. The maximum total score for BNIS assessment is 50 points, and scores of <47 points indicate cognitive dysfunction.

Assessment of ICF-classified activity (ADL)

AMPS process skills encompass the observable and temporally executed actions that an individual performs to enact tasks of ADL in a logical sequence. For example, process skills include the selection and use of appropriate tools and materials to complete a task, and adaptation of behavior or reactions when problematic situations are encountered. AMPS motor skills encompass the observable and goal-directed actions that an individual performs for locomotion of self or task objects. The linear ADL motor and ADL process ability measures are given in logits, where a higher score indicates greater ability. The AMPS instrument has a cut-off score of 1.0 and 2.0 logits for process and motor skills, respectively, indicating the ability to remain in independent living. A clinically relevant change in the AMPS score is 0.3 logits [20].

Study analyses

The patient population (n = 13) is described in terms of frequency, mean, SD, median, and range concerning age, gender, GCS, and injury type. Descriptive data for the DTI, BNIS, and AMPS analyses are provided in Table 2. To enable a visual analysis of the direction of change for DTI, BNIS, and AMPS scores, the change in units between 6 and 12 months is shown in Table 3, together with arrows signifying the direction of change (improvement vs. deterioration). The change is given as a raw score without consideration of its significance or clinical relevance, except for in the case of AMPS changes, which have a cut-off value for clinical relevance of 0.3 logits [20].

Statistical analyses were conducted by using the paired t-test for comparisons between DTI and AMPS assessments at different time points, providing a p-value and a confidence interval for each DTI/DTI and AMPS/AMPS comparison. The nonparametric Wilcoxon Signed Rank Test for paired analyses was used for the BNIS analysis, which has a sum score of ordinal data. In all cases, $p < 0.05$ was considered statistically significant.

Ethical considerations

This study was approved by the Regional Ethical Review Board in Gothenburg, Sweden. Informed consent was obtained from all study participants or their next of kin prior to study initiation.

Results

Since the current patient cohort was small and the results were sometimes contradictory, data from statistical analyses across groups required interpretation together with descriptive information regarding single patients.

BNIS, AMPS, and DTI data for each of the 13 patients included in the final analysis at the acute injury phase (assessment A1), 6 months post-injury (assessment A2), and 12 months post-injury (assessment A3) are presented in Table 2. Figure 1-5 presents scatterplots for the different measurements at 6 and 12 months with the results of the 13 patients indicated.

Results at the group level are discussed below for those eight patients with AMPS assessments at all three time points (patient population = P8; patient identification codes (ID) = A, B, C, F, G, H, I, and J in Table 1 and 2), and the five patients with AMPS assessments at A2 and A3 (patient population = P5; patient ID = D, E, K, L, and M in Table 1 and 2). However, the statistical analyses should be taken with caution, as the overall patient cohort and groups P5 and P8 were small, generating results with wide ranges.

DTI analysis of ICF-classified brain/white matter structure

In the P8 group one of the patients did not have a DTI assessment at A2 and A3 (ID = J). DTI analysis of the P8 group showed a mean FA value of 0.57 (SD, 0.05) at A1, 0.59 (SD, 0.03) at A2, and 0.60 (SD, 0.03) at A3 (n = 7 patients at each time point), whereas the mean trace values were 2.18 (SD, 0.23) at A1, 2.33 (SD, 0.09) at A2, and 2.47 (SD, 0.14) at A3. The five patients not well enough to be assessed at A1 (i.e., those included in the P5 group) had mean FA values of 0.53 (SD, 0.06) and 0.51 (SD, 0.04) at A1 and A2, respectively, and corresponding mean trace values

of 2.71 (SD, 0.35) and 2.79 (SD, 0.34). No significant longitudinal changes were observed for either P8 or P5 patients in the DTI evaluation, but the FA values tended to increase over time in the P8 group. By contrast, the FA values tended to decrease between 6 and 12 months in the P5 group. These findings are suggestive of a better outcome for patients in the P8 group, while the tendency toward increased trace values over time in both groups indicate that DAI may be associated with ongoing neuronal degeneration.

BNIS analysis of ICF-classified cognitive function

BNIS analysis of the P8 group revealed a median score of 43/50 (range, 30–48) at A1, 46.5/50 (range, 38–50) at A2, and 45/50 (range, 36–49) at A3. Meanwhile, the median BNIS scores in the P5 group were 36/50 (range, 21–40) and 38/50 (range, 18–43) at A2 and A3, respectively. Significant improvements were observed for the P8 group in terms of BNIS scores ($p = 0.017$) from the first assessment (A1) until the 6 month follow-up (A2), with seven study participants showing improvements from A1 to A2, and one participant showing the same score at both assessments. By contrast, no significant differences were discerned between 6 and 12 months post-injury for either P8 or P5 groups, which could stem from the diverse results seen at each time point for both groups. Two individuals in P8 showed improvements, one remained at status quo, and four showed a decline in BNIS scores between A2 and A3 (Tables 2 and 3), while three persons in P5 improved and two declined during the same study period.

AMPS analysis of ICF-classified ADL

Analysis of AMPS motor skills revealed a mean score of 1.98 (SD, 1.50) logits in the P8 group at A1. At the 6 and 12 month follow-up, the AMPS motor skill scores were 2.68 (SD, 0.66) and 3.19 (SD, 0.44) logits, respectively. Concomitantly, analysis of AMPS process skills showed a mean score of 1.38 (SD, 0.67) logits at A1, 1.65 (SD, 0.32) logits at A2, and 2.06 (SD, 0.48) logits at A3. The P5 group exhibited AMPS motor skill scores of 0.94 (SD, 1.29) and 0.67 (SD, 1.42) logits at A2 and A3, respectively, and AMPS process skill scores of 0.55 (SD, 0.90) and 0.91 (SD, 1.14) logits. A comparison of P8 and P5 subjects at 6 and 12 months showed significant inter-group differences in both assessment time points and both measures, as follows: AMPS motor skills at A2, $p = 0.019$ and A3, $p = 0.005$; AMPS process skills at A2, $p = 0.028$ and A3, $p = 0.040$.

Patients in the P5 group, who from the start presented with increased disability and could not be tested during the acute phase of injury, differed from patients in the P8 group in that they were also more impaired at each subsequent time point. P8 patients at A1 already showed a mean AMPS score above the cut-off level of 2.0 for motor skills and 1.0 for process skills. Between 6

and 12 months post-injury, all patients in P8 exhibited significant improvements in AMPS motor skills ($p = 0.019$), except for one individual, who exhibited an unchanged score. The process skill results were more diverse, as shown in Tables 2 and 3, with some P8 subjects showing an improvement and others showing a decline. Scores in the P5 group were below the cut-off levels for AMPS motor as well as AMPS process skills at both A2 and A3. Four of the five individuals in this group showed a tendency toward deterioration in motor skills between 6 and 12 months, but a simultaneous tendency toward improvement in process skills (Table 3).

Joint BNIS/AMPS analysis

According to the divergent pattern that emerged between P5 and P8 patients alike at 6 vs. 12 months in terms of BNIS scores, the subjects were re-grouped by BNIS results into "improved" and "deteriorated" groups for further exploration of the association between BNIS and AMPS scores between A1 and A2, and A2 and A3. An improvement in AMPS scores was found for all individuals from A1 to A2, regardless of BNIS scores, except for one person (patient B) with a decline in AMPS process skills, and another (patient G) with a decline in AMPS motor skills (Table 2).

The most interesting period of exploration seemed to be between 6 and 12 months after injury, due to the conflicting results on several measures. For example, DTI FA value changes as well as AMPS motor skill changes differed between the P8 and P5 groups at A2–A3. Furthermore, while stratified BNIS scores described a subgroup of patients with deteriorating outcomes, AMPS process skill scores showed a concurrent improvement in the same study participants (Table 3).

At 12 month follow-up, only three individuals (patients B, G, and H) had returned to work, with adaptations (i.e., changes in assignment at the same job, or changes in employment) (Table 3). Two (patients B and H) of these three individuals exhibited the highest BNIS scores at A1 (both patients, 48 points) (Table 2), and one (patient H) also presented with the highest BNIS score at A3 (49 points) (Tables 2 and 3). The latter was also the only patient with a BNIS score above the cut-off level at 12 months. However, at 12 months, several persons remained out of work who presented with BNIS scores that were as high as, or higher than, the scores of the other two study participants who had returned to work. The three persons employed at 12 month follow-up also demonstrated very good AMPS motor skills, but had only average AMPS process skills at A3 compared with the unemployed individuals (Table 3).

Discussion

Twenty-two patients who presented with DAI on CT scans during a 2 year period were enrolled in the present study. To ensure as "pure" a DAI representation as possible, we excluded all patients with an alternative explanation for affected consciousness and/or focal neurological symptoms after TBI. Since one person died during the course of the study and data were missing for certain other patients due to difficulties in performing the BNIS/AMPS assessments, the final study group was restricted to 13 persons. The small sample size was a great limitation of this pilot investigation, in terms of its ability to generate statistical significance and the possibility for generalization of the results. To overcome this limitation, we made an effort to systematize and assemble the data in such a way as to generate explorative, preliminary explanations for variations in the longitudinal changes of the three ICF domains: body structure, body function, and activity.

In an earlier report from our group, DTI data from the same patient cohort as that described herein were compared with DTI data from healthy controls [11]. The healthy controls exhibited a mean FA value of 0.6, while the TBI patients displayed significantly lower FA values, both during the acute phase and at 6 month follow-up. In addition, the control group exhibited a mean 6 month trace value of 2.21, which was significantly lower than that of the TBI group (2.63) due to a substantial increase in trace values (+0.43) in the latter between the acute injury phase and the 6 month assessment. The increase in trace values between assessments may reflect a continuous degenerative process, as described by others [2, 12]. However, this previous study did not include 12 month follow-up data for further evaluation of this proposal.

In the current study, the patient cohort was divided into two groups according to the capacity for testing during the acute phase of injury. Eight subjects who were able to perform the BNIS and AMPS tests at all three assessments were assigned to the P8 group, and five subjects who were unable to perform the tests acutely but could be tested at 6 and 12 months were assigned to the P5 group. A comparison between the two groups showed that the lower functioning in the P5 group again resulted in lower mean FA values, which provide a measure of body/brain structure. This result is in line with the findings of Spitz et al. [21], who showed a reduction in FA values for patients with moderate and severe TBI vs. healthy controls and individuals with mild TBI. The change in FA values toward higher readings for P8 patients between 6 and 12 months could indicate an improvement in the P8 group, but may alternatively suggest a pathologic process in the P5 group. Indeed, trace values were higher (indicating more pathology) in P5 vs. P8 subjects at study onset. Nonetheless, mean trace values increased as cognitive function decreased in P5 as well as P8 patients between 6 and 12 months, indicative of ongoing degeneration in both groups.

In an additional previous study of the same patient cohort, we found that half of the TBI subjects showed less favorable cognitive outcomes at 12 vs. 6 months after injury [9]. This observation is consistent with the findings of others and confirms the presence of an ongoing degenerative process [8]. In the present investigation, the P5 patients exhibited lower 6 month BNIS scores than the P8 patients, and this comparatively lackluster performance persisted until 12 months post-injury. However, the decline in BNIS scores between 6 and 12 months was evident for selected patients in both groups.

AMPS motor and process skill scores as a measure of activity disclosed a significant difference between the P8 and P5 groups at both 6 and 12 months, with P5 patients again presenting less favorable outcomes than P8 patients. The decline from A2 to A3 observed in body structure (DTI assessment) and body function (BNIS assessment) was not that apparent as observed in activity because patients in P8 made a significant improvement in AMPS motor skills between 6 and 12 months. On the other hand, 4/5 (80%) of the P5 patients revealed a decline in AMPS motor skill scores during the same assessment period. No significant changes in direction (either up or down) were observed for the corresponding AMPS process skill scores when averaged across all patients.

Several studies have indicated that despite progressive neuronal atrophy, clinical improvements can still occur in TBI patients [12, 13]. Possible explanations for this discrepancy are provided by the cognitive reserve theory and the theory of compensatory scaffolding [22, 23]. The cognitive reserve theory upholds the existence of compensatory activity in the brain, and proposes that factors such as education or inherent intelligence can mask cognitive deterioration [22]. With higher levels of cognitive reserve, potentially detrimental outcomes resulting from poor neuropsychological performance are mitigated. The compensatory scaffolding theory explains a different pattern of neural activity in the ageing brain as an adaptive mechanism of the brain. The adaptation consists of the development and use of complementary, alternative neural circuits to achieve a cognitive goal. According to both of these theories, clinical cognitive impairment is evident only when the need for compensation exceeds the level of cognitive reserve or the brain's capacity for plasticity and reorganization.

We next evaluated the current TBI patients with cognitive decline by organizing the relevant BNIS, DAI, and AMPS data into a table according to the direction of changes in the BNIS scores between 6 and 12 months. We previously described the decline in BNIS scores for six individuals included herein as a possible progression of DAI [9], in agreement with conclusions from other

studies [12, 13]. However, our present data showed a paradoxical improvement in AMPS process skills for most of the patients with declining BNIS scores (Table 3). AMPS process skills evaluate whether 1) a performance is logically sequenced, 2) the appropriate tools are selected, and 3) the subject is capable of modifying and adapting the performance when complications are encountered. Because these process skills are related to cognitive function, the apparent contradiction between BNIS and AMPS scores is somewhat surprising. A hypothesis that might account for this finding is that the BNIS reflects cognitive function and the influence thereupon of organic changes, while the AMPS reflects performance and the influence thereupon of compensatory strategies.

One may assume that all individuals use different cognitive strategies to manage their performance of ADL [14]. In some cases the use is purposeful and in some unconscious. However, some individuals utilize strategies effectively and consistently, and others not always as effectively. Strategies are described as tactics, procedures, or methods that a person may apply to acquire new skills or to cope with challenging situations, such as those that occur after a brain injury. Strategies help us to process information more deeply and to increase our ability to efficiently use and allocate cognitive resources.

Westwood [24] identified several different aspects of strategy use, including strategy use by the learner. The TBI patient is a particular type of learner, in that he or she must frequently reacquire many skills. Metacognition and self-regulation represent ways in which the learner can alter his or her approach to an enigma. After TBI, patients may achieve a better metacognitive awareness of his or her particular capabilities and limitations over time. If the person has a nurturing environment with stimulating and challenging activities, he or she will probably develop a better capacity for self-regulation. This proposal, as well as the suppositions behind the cognitive reserve theory, might explain why a current study patient, patient D, exhibited a longitudinal decline in BNIS scores but still revealed no improvement in AMPS motor or process skills (Table 3). According to the study results, this individual showed much lower cognitive function than the others, as well as great limitations in motor function and the ability to independently perform ADL. Therefore, we anticipate that this individual will exhibit an attenuated opportunity to develop strategy use and enhance metacognition in future endeavors, and to make use of different approaches to overcome obstacles.

Only three individuals in the present study returned to work within the first year after injury, indicative of the profoundly disabling consequences of DAI. Without a doubt, even those

patients with the best outcomes after TBI may experience difficulties in resuming employment (Table 3). Earlier studies on TBI concluded that it is difficult to find good predictors for a return to work because numerous and diverse psychosocial and injury-related factors interact to affect re-employment. These include environmental and economic circumstances, the type and duration of pre-injury employment, and personal characteristics [25-29]. Furthermore, the results of the present study suggest that a return to work may also depend on the extent of ongoing neurodegenerative processes, cognitive reserve, plasticity, and the use of compensatory strategies.

Longitudinally, the current study showed that many DAI patients eventually make progress in all three domains of the ICF. In some cases, an ongoing degenerative process in the white matter can be expected in MR-DTI and BNIS analyses of body/brain structure and body function from 6 to 12 months after injury. Because the same decline was not observed in the AMPS activity measure, we suggest that the use of cognitive strategies in combination with brain plasticity and cognitive reserve may compensate for DAI-induced deterioration. In this case, we conclude that it is of paramount importance to subject those patients at high risk of cognitive decline to early rehabilitative interventions that may offset eventual further disability.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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Figure legends

Figure 1. The figure illustrates DTI Fractional anisotropy (FA) values at 6 months and 1 year post injury for each of the participants. DTI measures water diffusion, its directionality in three dimensions (Trace), and diffusion anisotropy, which together allow for an indirect evaluation of the integrity of the white matter tracts. FA values range from 0 to 1, with lower values potentially representing a pathologic process. A coordinate above the reference line indicates a decrease in FA value between 6 months and 1 year post injury.

Figure 2. The figure illustrates DTI trace values at 6 months and 1 year post injury for each of the participants. Higher trace values might signify organic damage, and an increase in trace values between assessments could signify an ongoing neurodegenerative process. A coordinate below the reference line indicates an increase in trace value between 6 months and 1 year post injury.

Figure 3. The figure illustrates the BNIS scores at 6 months and 1 year post injury for each of the participants. The maximum total score for BNIS assessment is 50 points, and scores of <47 points indicate cognitive dysfunction. A coordinate above the reference line indicates deteriorated results between 6 months and 1 year post injury.

Figure 4. The figure illustrates the AMPS process skill scores, presented in logits, at 6 months and 1 year post injury for each of the participants. The AMPS process skill has a cut-off score of 1.0 logit indicating the ability to remain in independent living. A coordinate below the reference line indicates improvement between 6 months and 1 year post injury.

Figure 5. The figure illustrates the AMPS motor skill scores, presented in logits, at 6 months and 1 year post injury for each of the participants. The AMPS motor skill has a cut-off score of 2.0 logits indicating the ability to remain in independent living. A coordinate below the reference line indicates improvement between 6 months and 1 year post injury.

Table 1. The table shows all of the patients (age, 18–65 years; n = 22) admitted to the hospital from June 2006 through to September 2009 with suspected DAI and the clinical and radiological assessments each of the patients undertook acute (A1), at 6 (A2) and 12 months (A3) post-injury. Patients with AMPS assessments at A2 and A3 were included in the final analysis (grey rows).

NO	ID	Included	DTI A1	BNIS A1	AMPS A1	DTI A2	BNIS A2	AMPS A2	DTI A3	BNIS A3	AMPS A3
1	M	x	x	x	x	x	x	x	x	x	x
2			x								
3			x								
4	E	x	x			x	x	x	x	x	x
5				x	x	x	x	x	x	x	
6	H	x	x	x	x		x	x	x	x	x
7	A	x	x	x	x	x	x	x	x	x	x
8			x						x		
9	C	x	x	x	x	x	x	x	x	x	x
10	F	x				x	x	x	x	x	x
11	G	x	x	x	x	x	x	x		x	x
12			x	x	x	x	x				
13			x	x	x	x	x	x	x	x	
14			x	x	x	x	x		x	x	
15	L	x				x	x	x	x	x	x
16			x			x			x		x
17	D	x		x			x	x	x	x	x
18	K	x				x	x	x	x	x	x
19			x		x	x	x	x		x	
20	J	x		x	x	x	x	x	x	x	x
21	B	x	x	x	x	x	x	x	x	x	x
22	I	x	x	x	x	x	x	x	x	x	x

AMPS, Assessment of Motor and Process Skills; BNIS, Barrow Neurological Institute Screen for Higher Cerebral Functions;
DTI, diffusion tensor imaging; ID, patient identification code.

Table 2. Raw BNIS, AMPS, and DTI trace scores at various assessment time points for each study participant included in the final analysis.

ID	BNIS A1	BNIS A2	BNIS A3	AMPS process A1	AMPS process A2	AMPS process A3	AMPS motor A1	AMPS motor A2	AMPS motor A3	DTI trace A1	DTI trace A2	DTI trace A3
A	46	49	44.5	2.14	2.18	2.64	2.99	3.48	3.77	2.29	2.34	2.36
B	48	50	45	2.52	1.10	2.05	2.49	2.98	3.23	2.33	2.22	2.48
C	44	48	45	0.70	1.77	1.58	1.40	2.23	2.92	1.68	-	2.58
D	-	21	18	-	-0.20	-0.81	-	-0.52	-1.53	-	2.53	2.73
E	-	36	34	-	-0.27	0.79	-	0.00	1.10	-	3.15	3.10
F	30	38	36	0.51	1.43	2.31	-0.49	1.72	2.34	2.27	2.44	2.70
G	41	45	45	1.19	1.54	1.40	3.51	2.46	3.60	2.29	2.35	-
H	48	49	49	1.47	1.82	1.73	3.21	3.58	3.41	2.22	2.23	2.27
I	39	43	46	1.25	1.52	2.03	0.05	2.14	3.05	2.20	2.30	2.50
J	42	42	45	1.25	1.81	2.74	2.65	2.88	3.20	-	2.45	2.39
K	-	38	42	-	1.42	1.95	-	2.80	2.41	-	2.35	2.26
L	-	33	38	-	0.20	0.65	-	1.39	0.68	1.32	2.81	3.07
M	41	40	43	-	1.62	1.95	-	1.01	0.70			

AMPS, Assessment of Motor and Process Skills; BNIS, Barrow Neurological Institute Screen for Higher Cerebral Functions; DTI, diffusion tensor imaging; ID, patient identification code. The assessment time points were as follows: acute injury phase (A1), 6 months post-injury (A2), and 12 months post-injury (A3).

ID	Age	BNIS A3	AMPS process A3	AMPS motor A3	BNIS change A2–A3	AMPS process change A2–A3	AMPS motor change A2–A3	DTI Trace change A2–A3	Return to work	Employment before injury	Perceived problems at 1 year follow-up
♂ A	42	44.5	2.64	3.77	-5 ↓	0.46 ↑	0.29 NS	0.02 ↓		Local manager	Attention and executive function deficits, mood swings
♀ B	53	45	2.05	3.23	-5 ↓	0.95 ↑	0.25 NS	0.26 ↓	X	Administrator	Headache, memory deficits, difficulty keeping up with a conversation, fatigue
♀ C	20	45	1.58	2.92	-3 ↓	-0.19 NS	0.69 ↑	—		Clerk	Attention and memory deficits, impaired mood
♀ D	49	18	-0.81	-1.53	-3 ↓	-0.61 ↓	-1.01 ↓	0.20 ↓		Chef	Perseveration lapses, fatigue, lack of initiative, incontinency
♀ E	62	34	0.79	1.10	-2 ↓	1.06 ↑	1.10 ↑	-0.05 ↑		Biomedical scientist	Attention, memory, spatial orientation, and problem-solving deficits
♂ F	57	36	2.31	2.34	-2 ↓	0.88 ↑	0.62 ↑	0.26 ↓		Clerk	Fatigue, lack of initiative, impaired mood
♂ G	22	45	1.40	3.60	0 NS	-0.14 NS	1.14 ↑	—	X	Travel fitter	Attention, spatial orientation, and working memory deficits, fatigue, lack of initiative
♀ H	23	49	1.73	3.41	0 NS	-0.06 NS	-0.17 NS	0.04 ↓	X	Riding instructor	Headache, sleep problems, memory deficits
♀ I	22	46	2.03	3.05	3 ↑	0.51 ↑	0.91 ↑	-0.06 ↑		Assistant nurse	Fatigue, headache, mood swings, sluggish cognitive tempo, memory deficits

♂ J	19	45	2.74	3.20	3 ↑	0.93 ↑	0.32 ↑	-0.06 ↑		Student	Attention, problem solving, and learning deficits
♂ K	19	42	1.95	2.41	4 ↑	0.53 ↑	-0.39 ↓	-0.09 ↑		Student	Attention and memory deficits, sluggish cognitive tempo, impaired mood, mood swings
♂ L	25	38	0.65	0.68	5 ↑	0.45 ↑	-0.71 ↓	-0.26 ↑		Auto dismantler	Memory deficits, lack of motivation, impaired mood, sleep problems
♂ M	31	43	0.70	1.95	3 ↑	0.33 ↑	-0.31 ↓	—		Vehicle technician	Attention, problem solving, and planning deficits, sluggish cognitive tempo, fatigue