ORIGINAL ARTICLE doi: 10.2176/nmc.oa.2016-0049
Neurol Med Chir (Tokyo) 57, 94–100, 2017 Online December 22, 2016

Correlations between Cognitive Impairments and Employment Status in Patients with Diffuse Axonal Injury

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Abstract

Patients with diffuse axonal injury (DAI) may initially present with prominent physical impairments, but their cognitive dysfunctions are more persistent and are attributable to later unemployment. In this study, we analyzed how the findings of early and delayed neuropsychological assessments correlated with employment outcome of patients with DAI. A total of 56 patients with DAI without motor or visual dysfunction were included in this study. The neuropsychological battery consisted of the Wechsler Adult Intelligent Scale - Revised (WAIS-R), Wechsler Memory Scale - Revised (WMS-R), Trail Making Test (TMT), Wisconsin Card Sorting Test (WCST), and Word Fluency Test (WFT). This battery of tests was administered twice in early stage after injury and in later stage. The results of all of the neuropsychological tests improved significantly (P <0.001) between the early and later assessments. All scores other than TMT part A and B improved to the normal range (Z-score ≥ 2). The patient characteristics (age, gender, initial Glasgow Coma Scale, and duration of posttraumatic amnesia) had no relationship to the outcome. The results of TMT part B, however, were significantly correlated with employment outcome in both the early and later assessments (P = 0.01, 0.04). Given that TMT evaluates visual attention, we surmise that a lack of attention may be the core symptom of the cognitive deficit and cause the re-employment failure in patients with DAI. TMT part B in both early and later assessments has the potential to accurately predict chronic functional outcome.

Key words: diffuse axonal injury, neuropsychological test, employment outcome

Background

Diffuse axonal injury (DAI) is described as widespread axonal damage in the aftermath of acute or repetitive traumatic brain injury (TBI). Patients with this condition typically present with coma without focal lesions.[1,2] DAI is pathologically defined as axonal damage in multiple regions among the brain parenchyma and often impairs cognitive function by destroying neuronal connectivity.[3] Physical impairments may be prominent in the early phase after onset in patients with DAI, but cognitive and behavioral dysfunctions are more persistent and attribute more to the personal and social handicap of patients.[4,5]

Many studies have investigated the correlations between neuropsychological assessments and employment outcome in patients with TBI. One of the most important purposes of neuropsychological testing is to predict the long-term functional outcome. Yet, as of this writing, no adequate battery or optimal timing for neuropsychological assessment has been established. The timing of the neuropsychological assessment varies among the various clinical studies reported so far. In some studies, the assessment was performed at the resolution of post-traumatic amnesia (PTA), while in others it was performed at 3–6 months or as long as several years after the injury. The components of the battery for neuropsychological assessment also vary among practitioners. The subjects recruited in most clinical studies include all types of TBI and generally involving both the diffuse and focal type of pathology. Therefore, participants of previous studies have various dysfunctions, ranging from cognitive impairments to disabilities in motor, visual, or psychological functions. Thus, there has been no consensus on the feasible methodology for assessment depending on the variations in the neuropsychological status of patients. To solve such problems, we conducted a clinical study among a homogeneous group of patients by including only patients with DAI with only cognitive impairment but without physical disability.

Received February 15, 2016; Accepted August 12, 2016

The aim of this study is to clarify the correlations between neuropsychological assessments and employment outcome in patients with DAI without motor or visual dysfunctions and to find the most appropriate predictor for outcome in various neuropsychological batteries. We also attempted to analyze the natural time course of cognitive function in patients with DAI.

Methods

Participants

A total of 46 patients with DAI admitted to Japanese Red Cross Musashino Hospital between 1990 and 2012 were retrospectively analyzed. Neurosurgeons and radiologists diagnosed DAI based on computed tomography (CT), magnetic resonance imaging (MRI), and clinical symptoms. DAI was defined as the presence of lesions in lobar white matter, corpus callosum, or brainstem.

The following inclusion-exclusion criteria were applied: (1) between the ages of 16 and 75, (2) free of any large focal brain injury and treated conservatively (without craniotomy), (3) employed or in school at the time of injury, (4) followed up for more than two years, (5) able to cooperate for neuropsychological assessment (without consciousness impairments), (6) no motor dysfunction, (7) no visual dysfunction, (8) no significant history of previous neurological disorder, alcohol abuse, or psychiatric illness. Data on participants are summarized in Table 1. The duration of posttraumatic amnesia was divided into two groups: more than 24 hours and less than 24 hours.

Return to work was assessed when 2 years passed after the injury. Thirty-four patients (61%) were employed at this time point.

Table 1 Characteristics of the patients

Gender	Male = 41
	Female = 15
Age (years old)	42 ± 17
	(17–72)
GCS	11.2 ± 1.2
	(5–14)
Duration of PTA (>24 hours)	40 / 56
	(71%)
Employment	34 / 56
	(61%)
Early assessment (months after the injury)	1.8 ± 1.4
Delay assessment (months after the injury)	18.4 ± 6.5

Neuropsychological assessment

The neuropsychological assessment was performed twice, once early after the injury (1.8 ± 1.4 months) and once later (18.4 ± 6.5 months). The early assessment was intended within 3 months after the injury, and the later assessment was intended between 1 and 2 years after injury. Clinical psychologists at Japanese Red Cross Musashino Hospital performed all of the neuropsychological tests. The neuropsychological battery consisted of the following examinations: Wechsler Adult Intelligence Scale – Revised (WAIS-R), Wechsler Memory Scale – Revised (WMS-R), Wisconsin Card Sorting Test (WCST), Word Fluency Test (WFT: category only), Trail Making Test (TMT).

WAIS-R: WAIS-R is an intelligence test designed to measure cognitive ability in adults. The test obtains a verbal intelligence quotient (IQ), performance IQ, and full-scale IQ. All the three IQ scores were used in this study.[6]

WMS-R: WMS-R is designed to measure different memory functions in adults and is made up of 13 subtests. Among the subtests, Logical Memory (I & II) and Visual Reproduction (I & II) were used in this study.[7] Percentile scores were used in this study.

WCST: WCST is a measure of problem-solving and reasoning. The test produces various scores, but the total number of categories achieved was selected for use in the present investigation. Normative data stratified by age were cited from previous reports.[6]

TMT: TMT consists of two parts that each assesses visuomotor tracking, evaluate attention, and executive function. Normative samples quoted by Tombaugh were used in this study.[8]

WFT: WFT assesses verbal fluency and word generation. The only component of this test used in the study was an animal naming test. Normative data were taken from Tombaugh's previous reports.[9]

All of the data were converted to Z-scores [Z-score = (score – mean) / standard deviation] using normative data provided by the manufacturers of the tests and previous reports. A Z-score of -2 or less was judged to indicate persistent abnormality in the current study.

Ethics

The Ethical Committee of Japanese Red Cross Musashino Hospital approved this study.

Statistical analysis

Chronological changes in the results of the neuropsychological tests were analyzed by the paired t-test method with raw data. The effects of potential predictors were evaluated by univariate and multiple logistic regression methods. Potential predictors included patient characteristics (age, gender), injury severity variables (initial Glasgow

Coma Scale (GCS), duration of PTA), and the results of the neuropsychological assessment.

Results

Chronological change of the results of the neuropsychological assessment in patients with DAI

The scores of the entire neuropsychological assessment performed in the late time point significantly improved (*P* <0.001, Table 2) in comparison to those performed in the early time point. In the Z-score assessment, all the data improved to within the normal range (Z = −2 or more) except for TMT part A and B (Fig. 1).

Correlations between patient characteristics and employment outcome

The patients' characteristics (age, gender, initial GCS, and duration of posttraumatic amnesia) had no significant correlations with the employment outcome (Table 3).

Correlations between the early neuropsychological assessment and employment outcome

Among various scores obtained in psychological examination in the early time point, only the time required to complete TMT part B was found to be significantly correlated with the employment outcome (*P* = 0.01). None of the other scores significantly related to the outcome (Table 4).

Table 2 Chronological change of the score of the neuropsychological test

	Early	Late	*P* value
WAIS-R			
VIQ	82.3 ± 18.2	98.8 ± 17.9	<0.001
PIQ	84.3 ± 15.8	92.8 ± 16.2	<0.001
FIQ	81.9 ± 17.1	95.5 ± 16.6	<0.001
WMS-R			
Logical Memory I	39.3 ± 31.3	61.9 ± 30.6	<0.001
Logical Memory II	36.2 ± 33.3	60.2 ± 31.9	<0.001
Visual Reproduction I	31.3 ± 24.6	41.2 ± 30.1	<0.001
Visual Reproduction II	32.8 ± 29.5	49.4 ± 29.9	<0.001
Trail Making Test			
Part A	97 ± 44	90 ± 47	<0.001
Part B	156 ± 111	108 ± 48	<0.001
WFT (animal naming)	11.4 ± 4.0	13.8 ± 4.0	<0.001
WCST (category achieved)	3.3 ± 2.1	4.9 ± 1.7	<0.001

Relationships among the late neuropsychological assessment and employment outcome

In the psychological assessment performed in the later time point, the result was similar to the early time point study. Only the time required to complete TMT part B was significantly correlated with the employment outcome (*P* = 0.04). None of the other results had significant correlations with the outcome (Table 5).

Discussion

Neuropsychological tests are commonly used for various purposes in rehabilitation programs during both the early and late phases after TBI. One of the important purposes of neuropsychological assessment is to predict chronic functional and social outcome. Previous reports have suggested candidates for prediction markers such as age, initial GCS, duration of PTA, Perfomance IQ, Functional Independence Measure (FIM), psychological status, and attention. Yet, as of this writing, an optimal predictor has yet to be established.[5,6,10–14]

Previous reports examined patients with TBI with various pathologies collectively. The pathologies included various modes of brain destruction such as DAI, cerebral contusions, acute subdural hematoma, acute epidural hematoma, or mixture of these. Such strategy, however, hamper to eliminate the potential differences in clinical features, natural time course, and outcome among the different pathologies, and as a matter of course, failed to single out appropriate predictors of functional outcome. Cognitive improvements are sustained for longer in patients with TBI than in patients suffering from strokes such as intracerebral hematomas or cerebral infarctions.[5] In the present study, we eliminated pathology other than DAI and all subjects were confirmed as not having large focal lesions. We also eliminated patients who have motor or visual dysfunctions. Grauwmeijer et al. reported that Glasgow Outcome Scale, Barthel Index, FIM, and Functional Assessment Measure, indexes strongly influenced by motor function, and all correlated with employment outcome.[15] In the present study, we centered our focus on the effects of cognitive function by excluding patients with motor and visual dysfunctions as both factors should influence both on the scores of neuropsychological tests and employment outcome.

In the comparison between the results of the early and late neuropsychological tests, all cognitive functions improved significantly in our study. The pattern of cognitive improvement is useful for characterizing cognitive impairment after brain injury and can help physicians to discriminate other deficits

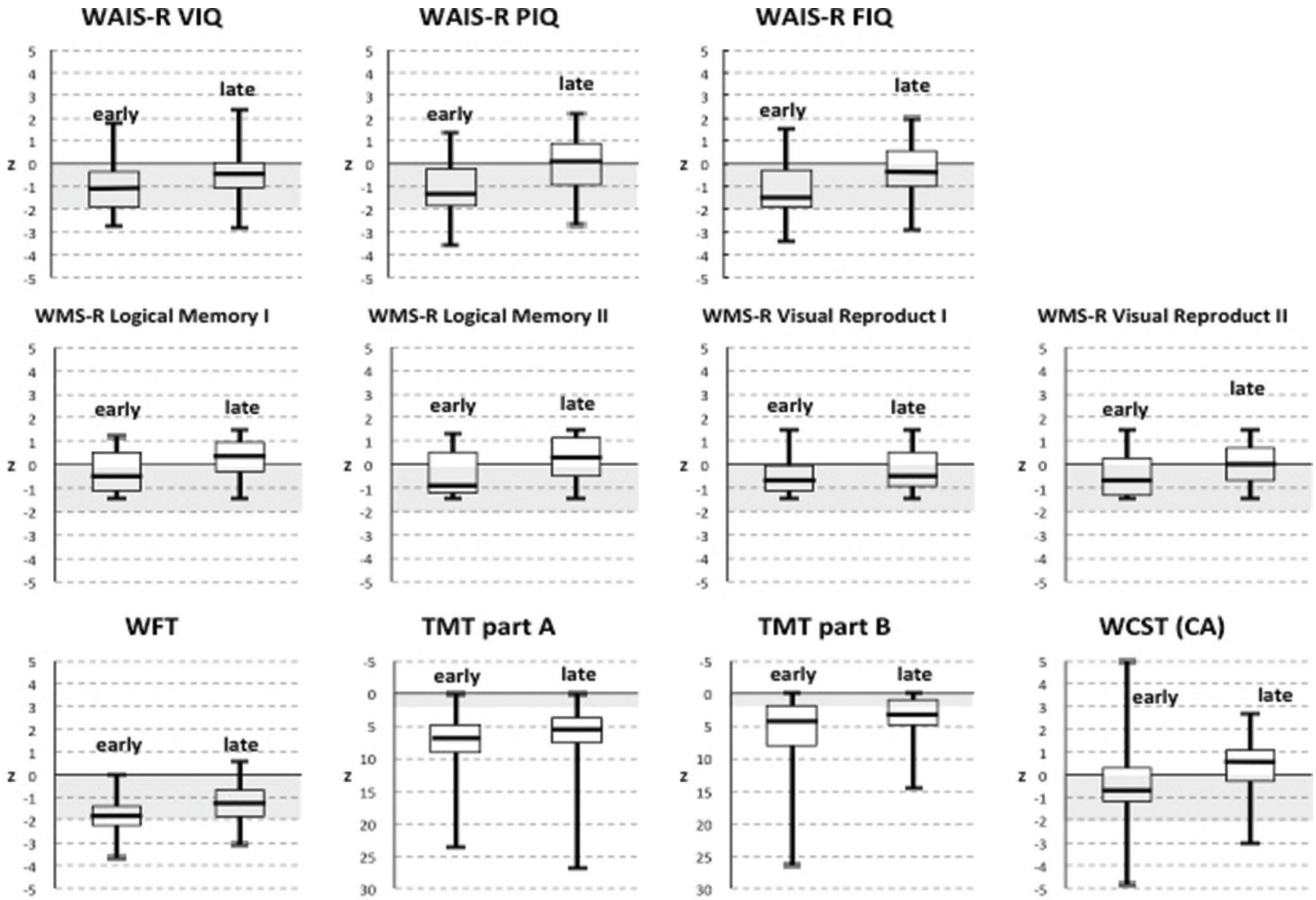

Fig. 1 Box-and-whisker plot of the Z-scores for each neuropsychological test. The Z-scores for TMT part A and B did not reach the normal ranges.

Table 3 Correlation between patient characteristics and employment outcome

	Re-employment (*N* = 34)	Unemployment (*N* = 22)	*P* value
Gender	Male = 25	Male = 16	0.94
	Female = 9	Female = 6	
Age (years old)	43.1 ± 3.1	40.5 ± 3.8	0.59
GCS	11.8 ± 3.6	12.2 ± 2.6	0.59
Duration of PTA (> 24 hours)	22/34 (65%)	18/22 (82%)	0.16

such as Alzheimer's disease or vascular dementia. The scores for all of the neuropsychological tests but TMT part A and B improved to the normal range (Z-score ≥ 2). The Trail Making Test is a neuropsychological test to evaluate visual attention and task switching. The subject is instructed to connect a set of 25 dots in sequential order as quickly as possible without sacrificing accuracy. There are two parts to the test: in part A, the targets are all numbers (1, 2, 3, etc.); in part B, the subject alternates between numbers and letters (1, A, 2, B, etc.). The test can provide information about visual search speed, scanning, processing speed, and mental flexibility, as well as executive function. As TMT part B is a more complex task than A, it could detect abnormality in visual attention with higher sensitivity than A. Our results suggested that the core cognitive dysfunction in patients with DAI was a disorder of attention.

Many studies have found little or no association between employment outcome and the initial GCS or duration of PTA, although the duration of PTA has been consistently found to be a stronger predictor of outcome than the initial GCS.[15–18] Brown et al. reported that the duration of PTA predicted total FIM one-year after employment and global outcomes.[17] Nakase-Richardson et al. reported that most individuals with PTA durations of less than 14 days had favorable 1-year outcomes (68% productive) and individuals with PTA durations of more than 28 days had worse outcomes (18% productive).[18] The employment outcome in our results showed no relationship with the initial GCS or PTA duration. Most of the patients in our study suffered mild-to-moderate DAI and presented with a somewhat higher initial GCS

Table 4 Correlation between early assessment and employment outcome

Neuropsychological test (Z score > −2)	Re-employment (*N* = 34)	Unemployment (*N* = 22)	*P* value
WAIS-R			
VIQ	29 (85%)	18 (81%)	0.71
PIQ	27 (79%)	20 (91%)	0.26
FIQ	29 (85%)	16 (72%)	0.25
WMS-R			
Logical Memory I	31 (90%)	18 (82%)	0.3
Logical Memory II	29 (86%)	18 (81%)	0.72
Visual Reproduction I	32 (93%)	20 (91%)	0.64
Visual Reproduction II	26 (76%)	19 (86%)	0.38
Trail Making Test			
Part A	1 (4%)	0 (0%)	0.41
Part B	14 (40%)	1 (6%)	0.01
WFT (animal naming)	22 (64%)	9 (43%)	0.08
WCST (category achieved)	20 (60%)	18 (84%)	0.07

Table 5 Correlation between late assessment and employment outcome

Neuropsychological test (Z score > −2)	Re-employment (*N* = 34)	Unemployment (*N* = 22)	*P* value
WAIS-R			
VIQ	32 (95%)	21 (95%)	0.82
PIQ	31 (91%)	21 (95%)	0.54
FIQ	31 (91%)	21 (95%)	0.54
WMS-R			
Logical Memory I	32 (93%)	22 (100%)	0.25
Logical Memory II	32 (93%)	22 (100%)	0.25
Visual Reproduction I	32 (93%)	20 (91%)	0.65
Visual Reproduction II	32 (93%)	21 (95%)	0.82
Trail Making Test			
Part A	1 (4%)	0 (0%)	0.41
Part B	16 (48%)	4 (18%)	0.03
WFT (animal naming)	27 (79%)	13 (61%)	0.1
WCST (category achieved)	30 (88%)	22 (100%)	0.09

compared to earlier reports. Due to our exclusion criteria, none of our patients had motor disabilities or were unable to cooperate or follow instructions in the neuropsychological assessments. Our exclusion of severe patients with TBI may explain why the initial severity did not correlate with the functional outcome. In our mild-to-moderate patients with DAI, the patient characteristics and initial coma severity could not predict the chronic functional outcome.

The TMT part B score proved to be a potentially reliable predictor of chronic employment outcome in our study. Finnanger et al. reported that executive dysfunction and attention problems detected by different neuropsychological tests affected an individual's ability to resume independent living and employment regardless of injury severity or age.[19] Williams et al. also showed the utility of TMT part A and B as predictors of an employment outcome, and their results support the validity of our data.[11]

Memory function contributed to an individual's return to work in the report from Ryu and Kai, while our data showed no significant relationship between memory function and return to work.[12,14] The evaluations of the memory function by WMS-R Logical Memory (I & II) and Visual Reproduction (I & II) in our study indicated a return to near normal ranges. This discrepancy may have stemmed from differences in severity and uniformity among our participants. Other candidate predictors are intelligence scales. Kai et al. mentioned that a patient's full-scale IQ is an important indicator in returning to work under conditions of competitive employment.[14] Yet, many previous studies were consistent with our study in showing no relationships between intelligence scales and outcomes.[5] More detailed investigation of WAIS-R, such as subindex analysis, and discrepancy analysis, could show the possibility as the prediction marker. WCST is a measure of problem-solving and reasoning, and sometimes used as a part of the assessment battery of patients with TBI. However, no previous reports showed the correlation among WCST and working outcome, as well as our results.

The adequate timing of neuropsychological assessment is another unsolved problem in the prediction of social outcome.[5] Cognitive function in the early period after injury is not strongly correlated with the prognosis of social outcome in earlier reports. In some of the previous studies, the results of cognitive function evaluations in the acute phase were uncorrelated with social outcome in the long term. Other reports did show potential correlations between the two, but the predictive factors were different.[5] Some studies revealed no correlations among the results of late cognitive evaluations and employment outcome. In our results, abnormal performance on TMT part B significantly correlated with employment outcome in both the early and later phases after injury. Further, none of the other test results influenced the outcome in either period. Only a few reports have performed neuropsychological tests repeatedly on the same patients.[19,20] Our results suggested that timing is not important once consciousness has been recovered. Though difficult to confirm, the evidence suggests that early (provided that at least several months have passed since the injury) and late periods are both appropriate for assessing and predicting chronic functional outcome.

Return to employment has been used as one of the common and traditional indicators of functional outcome. Employment is an outcome valued by society and can be more objectively assessed than personal independence. Yet the prediction of employment outcome is often confounded by various influential factors not associated with the patient's neurologic status, such as the pre-injury employment status, demographic variables, availability of environmental supports, and family support. Though job type might be one of the non-injury-related factors that influenced the employment outcome, we did not investigate the correlation in this study. The criteria for successful vocational outcome may be misleading, for example, if one neglects to discriminate between those who return to activity as homemakers and those who transition from outside employment to homemakers. This error becomes particularly important when the heterogeneous demographics and injury severity levels of the TBI population are taken into account. Confounding factors of this type might partly explain why no adequate prediction markers have been established. Further investigation in a different population will have to be performed before the validity of TMT as a predictor can be confirmed.

Psychiatric symptoms such as depression and anxiety are widely recognized as chronic symptoms of traumatic impairments. Wagner et al. identified psychiatric symptoms as a risk factor of unemployment.[21] We attempted no psychological examinations in our own subjects, which limits our study in one respect.

In these days, radiological diagnostic technique advanced dramatically, destructed brain network visualized in each patient clearly. Radiological findings might have the strong correlation between the neuropsychological results and employment outcome. However, we did not investigate the influence of radiological findings. The participants of this study were recruited for more than 20 years, radiological diagnostic technique and equipment has dramatically advanced and changed, which limits our study. Further investigation with detailed radiological inspection may clarify the mechanism of cognitive impairment and cause of later impairment.

This study focused the relationships among cognitive dysfunction and social outcome in patients with diffuse brain injury. We disregarded the influence of focal brain destruction and the effects of impairments in non-cognitive functions. The limited scope and homogeneous population we selected for this study necessarily led to conclusions different from those reported in the past. We showed that dysfunction of attention is a core reason for unemployment in patients with DAI. This study was retrospective, so further prospective investigation may be required to clarify the cognitive problems of diffuse brain injury.

Conclusion

We have investigated the correlations between neuropsychological assessment and employment outcome in pure patients with DAI without motor or visual dysfunctions. The results of all of the neuropsychological tests improved to normal range, except for TMT part A and B. The TMT part B score was the only result to correlate with employment outcome in both the early and later assessments. The employment outcome of patients with DAI may depend on fully functional attention. TMT, therefore, proved to be a useful predictor of employment outcome in our study population.

Acknowledgement

The authors thank the General Insurance Association of Japan for supporting this research.

Conflicts of Interest Disclosure

All authors report no conflict of interest related to this manuscript.

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