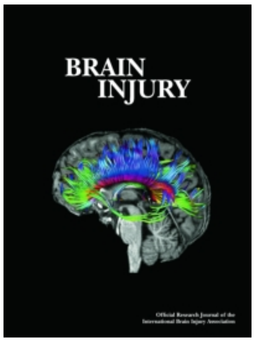

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Relationships between neuropsychological impairments and functional outcome eight years after severe traumatic brain injury: Results from the PariS-TBI study

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ABSTRACT

Background/objectives: The objective was to assess the relationships between neuropsychological impairments, functional outcome and life satisfaction in a longitudinal study of patients after a severe traumatic brain injury (TBI) (PariS-TBI study).

Patients: Out of 243 survivors, 86 were evaluated 8 years post-injury. They did not significantly differ from patients lost-to-follow up except for the latter being more frequently students or unemployed before the injury.

Methods: Outcome measures included the Glasgow Outcome Scale-Extended (GOS-E), a functional independence questionnaire, employment, mood, fatigue and satisfaction with life. Neuropsychological outcome was assessed by two ways: performance-based outcome measures, using neuropsychological tests and patient and relative-based measures.

Results: Neuropsychological measures were not significantly related to initial injury severity nor to gender, but were significantly related to age and education. After statistical correction for multiple comparisons, cognitive testing and cognitive questionnaires were significantly correlated with most outcome measures. By contrast, satisfaction with life was only related with patient-rated questionnaires. A regression analysis showed that the Trail-Making-Test-A was the best predictor of functional outcome, in addition to education duration.

Conclusions: Cognitive measures, particularly slowed information processing speed, were significant indicators of functional outcome at a long-term post-injury, beyond and above demographics or injury severity measures.

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Severe traumatic brain injury (TBI) can result in long-lasting cognitive deficits, associated with behavioral and personality changes and mood disturbances (1). Patients with severe TBI may show difficulties in social and family interactions, in their ability to study or to return to a productive ability. Previous research showed that long-term functional outcome results from a complex combination of injury-related factors (severity of injury) and demographic factors (age, gender, educational level) ((2) for a review). Psychosocial trajectories after TBI are complex and global outcome may vary significantly over time (3). Some patients may continue to improve at a long-term post injury. For example, Forslund et al. (3) reported that, between 5- and 10-year follow-up, 37% of a sample of patients with moderate to severe TBI had deteriorated, while 7% had improved. More optimistic findings were obtained in the PariS-TBI study, as 40% of participants continued to improve from 1- to 4-year and 52% from 4- to 8-year after a severe TBI (4,5). However, a trend for long-term memory decline has been reported in a minority of patients (6). Such trajectories may be influenced by patient-related variables but also by environmental and organizational factors. Indeed, the provision of community-based support has been found associated with long-term benefits (4,7).

The predictive value of cognitive abilities on functional outcome remains however debated (8–14). This is an important issue, as most practitioners involved in TBI care commonly use neuropsychological testing to predict a patient's ability in everyday life.

A number of studies found significant relationships between cognitive testing and functional outcome. Williams et al. (8) found, in a longitudinal study of 288 adults with TBI or various severity, that cognitive evaluations uniquely contributed to outcome predictions of functional disability (including return to work), even after considering demographic, injury severity and CT characteristics. However, neuropsychological testing did not improve the prediction of life satisfaction. In a similar way, Hanks et al. (9) in a cross-sectional study of 377 patients

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1–25 years post TBI found that neuropsychological test scores from a brief outpatient battery represented independent predictors of disability, need for supervision and employment, in addition to demographic and injury characteristics. Bercaw et al. (10) also showed that neuropsychological test scores one-year post injury were predictive of 2-year functional outcome. Ponsford et al. (11) assessed 60 patients with mild to severe TBI 10 years after the injury. They found that performances on tests of information processing speed, attention, memory, and executive function were significantly predictive of outcome using a dichotomized Glasgow Outcome Scale-Extended (GOS-E) (15). The cognitive measure that obtained the largest effect-size was slow processing speed, as measured on the Digit Symbol Coding subtest. In addition, Wilson et al. recently reported a study based on a large (n = 1554) sample of patients with mild to severe TBI, from the multicenter European CENTER-TBI study (14). They used one-way analyses of covariance, adjusted for age, sex and education, to compare cognitive performance across the different GOS-E categories and found small to medium effect-sizes. The greatest effects involved speed of processing and learning and memory. There were large deficits of performance for patients with Severe or lower Moderate Disability (GOS-E scores 3–5) while cognitive performance was surprisingly similar (mildly impaired) across the three higher levels of functioning (upper Moderate Disability or Good recovery).

However, contrasting results have also been reported. Wood & Rutterford (12) found, in a sample of 131 participants more than 10 years post-injury, that cognitive variables had a limited capacity to predict very late outcome. The only cognitive domain to make a significant contribution to outcome was working memory, which predicted community integration, satisfaction with life, and depression. However, this sample included a relatively high number of participants with mild or moderate TBI (the median PTA duration was 7 days).

Allanson et al. (13) recently reported the results of a meta-analysis on neuropsychological predictors of outcome after TBI. Seven studies were selected, which included either the GOS-E (15), or the Disability Rating Scale (DRS) (16) as outcome measure. Large and statistically significant correlations were found between functional outcome measures (mainly with the GOS-E) and a number of neuropsychological dimensions: immediate and delayed verbal memory, visuo-spatial construction, set-shifting, and generativity. Multiple regression analysis showed that these neuropsychological dimensions were all significant independent predictors of outcome, except for immediate verbal memory, and that they explained 31% of the variance of the GOS-E.

Taken together, the findings from these different studies all suggest that neuropsychological tests add unique predictive information for long-term functional outcomes after TBI, and that there is a need to use a combination of tests addressing different cognitive dimensions to assess outcome.

However, most of the above-referenced studies included a wide range of TBI severity (including patients with moderate or even mild TBI). The present study is among the few to examine a homogenous sample of patients with severe TBI as much as eight years post-injury. The aim was to explore the relationships between neuropsychological impairments and functional and social outcome at a long term after a severe TBI. The PariS-TBI study (17,18) is a prospective inception cohort study of patients with severe TBI in the Parisian area which offers a unique opportunity to address this issue in a homogeneous sample of patients. Global data on 8-year outcome have been previously reported (5,19). To summarize: cognitive complaints were reported by about 70% of the sample, whereas motor or balance problems were reported by less than half of the patients, and were severe in only a minority of cases (about 10%); the majority of patients (37%) were in the upper Moderate Disability category according to the GOS-E, 45.1% (and 48.7% of patients aged under 65) were employed in a productive job, and the majority of subjects (90.2%) were independent for elementary daily-life activities while 20% to 50% needed help for more complex tasks (taking public transport, writing a letter or financial and administrative management).

Methods

Participants and design of the PariS-TBI study

The present study was part of a larger regional prospective inception cohort study called PariS-TBI, which was undertaken in 2005 in Paris city and its suburbs. Consecutive patients were included by mobile emergency services of the area over a 22-month period. Criteria for inclusion were patients aged 15 or more with a severe TBI (lowest Glasgow Coma Scale (GCS) score before hospital admission of 8 or less, in the absence of other causes of coma). Data from intensive care units (ICU) to home discharge were collected prospectively.

A total of 504 patients were included. Subjects were mainly men (77%), mean age was 42 ± 20 years (min-max = 15–98). Main causes of injury were road traffic accident (53%) and falls (35%). There were 257 patients who survived after the acute stage, and 14 patients died later, after discharge, so there were 243 surviving patients eight years post-injury. From this initial sample, 134 were evaluated at one-year outcome (20), 147 could be evaluated for the four-year follow-up (18), and 86 patients attended 8-year follow-up (19). Some of these patients however did not complete all the tests or questionnaires for various reasons, related to time available or to fatigue. As can be seen on there were fewer missing data for questionnaires, which were completed by 76 to 78 patients than for cognitive tests, which were completed by about 54 patients (although this depended on the test). Forty-eight relatives were available to rate the subjective questionnaires. The present study is based on the results of the eight-year post-injury assessment. Patients and their relatives were contacted by telephone and mail, in order to schedule a face-to-face interview with a trained neuropsychologist (GN).

Materials

Baseline demographic, and injury severity measures

Socio-demographic characteristics included age at time of injury, gender, and years of education. These data were included in the original database, and completed if necessary during the eight-year interview.

Brain injury severity was assessed using the following variables: last GCS score before arrival at the hospital (without any previous sedation or after a transitory stop of sedation), time to follow commands, length of stay in intensive care unit (ICU), and disability upon discharge from ICU, as measured with the Glasgow Outcome Scale (GOS) (21). Duration of post-traumatic amnesia could unfortunately not be included in the model, as there were too many missing data.

Assessment of functional outcome

The choice of outcome measures was based on current knowledge of outcome after severe TBI. Some of them were part of the NINDS Common Data Elements for TBI (22), but other measures were selected here as they have been used at earlier stages of the PariS-TBI study, or because they were available in the French language. Global functional outcome was assessed using the GOS-E (15), which ranges from death to Upper Good Recovery on an eight-point scale. Scoring of the GOS-E was made by one of the authors (GN), based on the French translation of the structured interview proposed by Wilson et al. (15). Return to a productive employment was also recorded. Productive employment was defined here as any kind of paid employment, either full-time or part-time, in the open market or in a sheltered environment (not including studying). As mentioned earlier, more detailed information about vocational status of the present sample has been reported previously (19). In addition, a questionnaire assessing independence in activities of daily living was used. This questionnaire is a slightly modified version of the "activities of daily living" section of the European Brain Injury Society (EBIS) Head Injury Evaluation Chart, which has been used in previous research and has been found sensitive to TBI (23). The original chart includes 12 items, 6 related to basic and 6 to advanced activities of daily life. In the present study, to simplify data collection, the most relevant activities were retained, as follows: four out of the six basic activities of daily life were grouped into one single question (covering dressing, grooming, toileting and indoor walking); and four out of six advanced activities were retained: using public transportation; writing a letter; dealing with financial and administrative matters; driving a car or a motorcycle. For each of these tasks, and in accordance with the original EBIS chart, a 4-point Likert-type scale was used ranging from 0 (total independence) to 3 (inability to complete the task alone). The total score was used here (range: 0–15, higher scores indicating poorer independence).

Assessment of mood, fatigue and quality of life

Mood was assessed with the Hospital Anxiety and Depression Scale (HADS) (24) which has two sub-scores for anxiety (max = 21) and depression (max = 21), and a global score (max = 42). Mental fatigue, which may impact cognitive performance and behavior, was assessed through the Fatigue Severity Scale (FSS) (25), which has previously been found sensitive to brain injury. The FSS measures impact of fatigue on daily functioning and the distress caused by fatigue. It includes nine items related to fatigue over the past 2 weeks, which are rated on a Likert-type 7-level scale. Higher scores indicate higher subjective fatigue. Quality of life was assessed using a visual-analog scale where patients were asked to rate their subjective overall satisfaction with life (range: 0, very poor satisfaction to 10, highest satisfaction possible).

Assessment of neuropsychological impairments

In order to assess problems in the neuropsychological domain, two sets of measures were taken: performance-based measures, relying on widely used neuropsychological tests, and patient- and/or relative-based measures, including questionnaires on changes that occurred in everyday life since the injury.

Speed of processing was assessed using the Processing Speed Index (PSI) from the Wechsler Adult Intelligence Scales-Fourth Edition (WAIS-IV) (26). The PSI is derived from two subtests, the mean value of the standardized score in healthy individuals is 100 (SD = 15).

Verbal learning was assessed with the French version of the California Verbal Learning Test (CVLT) (27). This test involves the oral presentation and recall of 16 words across five trials, followed by a single presentation of a second, interfering, 16-word list, and by short- and long-term recall of the first list. Free recall was followed by a cued recall condition, where patients were given the words' semantic categories. Scores used here were standard scores of the first-list and raw scores (as no standard scores were available for these measures in the French version) of short-term free recall, short-term cued recall, long-term free recall, and long-term cued recall of the first list.

Mental flexibility was assessed using the Trail Making Test (TMT) (28,29), parts A and B. Part A required the subject to draw as fast as possible lines to connect consecutively 25 numbered circles on an A4 paper sheet. In part B, they had to connect consecutively numbered (1 to 13) and lettered (A-L) circles by alternating between the 2 sequences. Time of completion of forms A and B, and interference time (B minus A) were measured.

Planning and multitasking were assessed using the Modified Six-Element test (28,30). Participants were instructed to complete six simple tasks within a given time limit (10 minutes). They were explicitly instructed that they had to complete at least some part of each one of the six subtasks, and that they were not allowed to do two subtasks of the same type immediately one after the other. The score was a global score (rank score) calculated with the following formula: the number of tasks correctly attempted minus the number of tasks with rule break (range: 0–6).

Behavioral changes were assessed using the Dysexecutive Questionnaire (DEX) (30,31). The DEX is a 20-item questionnaire, completed by the patient and by a relative, measuring changes in everyday life as a result of executive dysfunction (score range = 0–80, higher scores indicating more severe impairments). A subjective assessment of complaints related to everyday life was obtained through the Brain Injury Complaint Questionnaire (BICoQ) (32,33). The BICoQ includes 25 yes/no questions addressing a wide range of complaints commonly reported by patients with acquired brain injury, related to cognitive processes, fatigue, mood, sleep, somatic disorders and behavior (irritability/apathy). This questionnaire also includes a version for relatives, and a measurement of the difference between patients' and relatives' ratings to assess self-awareness.

Statistical analyses

Statistical analyses were computed with SPSS 22 statistical software (IBM SPSS Statistics, IBM Corporation, Chicago). Categorical variables are shown as numbers and percentages, continuous variables are expressed as means and standard deviation (SD). Relationships between neuropsychological testing and questionnaires (DEX and BICoQ) on the one hand and outcome measures on the other hand were assessed using Spearman's Rho correlation coefficient, due to the distribution of data, or with one-way ANOVAs for categorical variables (gender, return to work). To minimize type I error on multiple comparisons, the alpha level was arbitrarily set at $p < .01$. A regression analysis was then computed to assess the determinants of the GOS-E. We used pairwise deletion when there were missing data in neuropsychological assessment.

Ethical aspects

The research was completed in accordance with the Helsinki Declaration. Patients and their families had been informed about the purpose of the PariS-TBI observational study upon inclusion in the database. Before the 8-year assessment, patients and their proxies were given written and oral information and gave their oral consent to participate, in accordance with French legislation. The study was approved by the local ethics committee (Comité de Protection des Personnes, CPP XI, Poissy-Saint Germain hospital) and by the Consultative Committee for Treatment of Health Research Information (CCTIRS, from the French Ministry of Health). The study was recorded in ClinicalTrials.gov in August 2011 (identifier: NCT01437683).

Table 1. Demographics, injury severity and 8-year functional status, mood, fatigue and QoL.

Patients' characteristics	Mean (SD) or n (%)
Demographics	
Age (years) (n = 86)	41.8 (13.6)
Years of education (n = 81)	12.2 (3.9)
Gender (male) (n = 86)	68 (79.1%)
Pre-injury alcohol abuse (n = 82)	17 (20.7%)
Injury severity	
GCS (n = 85)	5.8 (1.8)
Time to follow command (n = 75) (days)	12.4 (10.6)
LOS in ICU (days) (n = 86)	28.8 (23.8)
GOS upon ICU discharge (n = 75)	3.8 (0.8)
8-year outcome	
GOS-E (n = 86)	5.9 (1.5)
Independence score (n = 82)	3.3 (3.2)
Productive work (n = 82)	37 (45.1%)
HADS (n = 76)	11.6 (8.3)
FSS (n = 78)	5.4 (3.3)
QoL (n = 76)	6.5 (1.9)

LOS = length of stay; ICU = Intensive Care Unit; GOS = Glasgow Outcome Scale; GOS-E = Glasgow Outcome Scale – Extended; HADS = Hospital Anxiety and Depression Scale; FSS = Fatigue Severity Scale; QoL = Quality of Life

Table 2. Results of neuropsychological testing and subjective questionnaires.

Tests/scales	Mean (SD)
Neuropsychological testing	
PSI (n = 53)	87.0 (15.7)
CVLT-first list total standard score (n = 54)	-1.6 (1.7)
CVLT-short term free recall (n = 54)	8.0 (4.2)
CVLT- short term cued recall (n = 54)	9.1 (3.7)
CVLT- long term free recall (n = 53)	8.4 (4.3)
CVLT- long term cued recall	8.98 (4.0)
TMT-A (secs) (n = 56)	44.07 (24.0)
TMT-B (secs) (n = 54)	103.9 (59.1)
TMT interference time (secs) (n = 54)	63.6 (45.1)
Modified SET rank score (n = 34)	-1.1 (5.8)
Questionnaires	
DEX-patient (n = 76)	16.6 (13.7)
DEX-relative (n = 47)	24.1 (16.9)
DEX-difference (n = 41	1.2 (21.2)
BICoQ-patient (n = 76)	10.4 (6.2)
BICoQ-relative (n = 48)	13.4 (6.1)
BICoQ-difference (n = 41	0.9 (5.6)

PSI = processing speed index (standard score from the WAIS-IV); CVLT = California Verbal Learning Test; TMT = Trail Making Test; SET = Six-element test; DEX = Dysexecutive Questionnaire; BICoQ = Brain Injury Complaint Questionnaire.

Results

Patients' baseline characteristics

There were 86 patients who attended 8-year follow-up. Patients' characteristics are shown on Table 1. The mean delay since the TBI was 98.5 months (SD: 8.65). Four of the 86 patients refused to complete the totality of the questionnaires. According to the GOS-E, 17 (19.7%) patients had a Severe Disability (respectively 7 and 10 in the lower and upper categories), 42 (48.8%) had a Moderate Disability (11 lower and 31 upper) and 27 (31.4%) patients obtained a Good Recovery (15 lower and 12 upper). Patients' performance on neuropsychological testing and the results of the two questionnaires are presented in Table 2.

Patients included in the present study were compared with lost-to-follow up individuals. There was no statistically significant difference between these two groups regarding age, gender, severity of injury, disability (as assessed with the GOS) upon discharge from the ICU, alcohol abuse or marital status (living alone or not). However, included patients had a significantly higher educational level (12.2 ±3.2 vs. 11.0 ± 2.6 years of education) and were more often employed pre-injury (72.0% vs. 57.6%) than patients lost to follow-up (both $p < .01$).

Relationships between neuropsychological measures (tests and questionnaires) and demographic data

As can be seen on Table 3, the effect of gender (as assessed with one-way ANOVAs) was statistically significant for only one cognitive variable, the rank score at the Modified Six-Element Test, due to a better performance for women. Two neuropsychological measures were significantly related to age: CVLT-first list total standard score (surprisingly a positive correlation, i.e. better scores for older patients), and time of completion of TMT-A, due to a slower performance for older patients. Education duration was significantly correlated with most memory scores and with all scores derived from the TMT, due to a better and faster performance for more educated patients. Education duration

Table 3. Relationships between neuropsychological data and outcome variables.

	Gender (F)	Age (Rho)	Education (Rho)	GCS (Rho)	GOS ICU discharge (Rho)	HADS (Rho)	FSS (Rho)	QoL (Rho)	GOS-E (Rho)	FI (Rho)	RTW (F)
Neuropsychological testing											
PSI (n = 53)	1.1	.21	.49**	.31	.13	−.20	−.34	.03	.32	−.50**	3,6
		(−.05;.46)	(.27;.68)	(−.04;.48)	(−.14;.43)	(−.45;.07)	(−.63;-.18)	(−.23;.31)	(.09;.57)	(−.72;-.33)	
CVLT-first list total standard score (n = 54)	0.5	37**	29	16	31	−.32	−.35**	14	21	−.30	30
CVLT-short term free recall (n = 54)		(.04;.53)	(.02;.52)	(−.14;.38)	(−.01;.52)	(−.53;-.04)	(−.64;-.21)	(−.13;.4)	(−.03;.48)	(−.59;-.13)	
CVLT- short term cued recall (n = 54)	4.9	15	35**	07	17	-.17	-.34**	09	27	-.41**	9.1**
CVLT- long term free recall (n = 53)		(−.14;.39)	(.07;.55)	(−.23;.3)	(−.1;.45)	(−.39;.14)	(−.6;-.14)	(−.2;.33)	(.06;.54)	(−.58; −.11)	
CVLT- long term cued recall	4.8	14	35**	17	15	-.18	-.28	03	25	-.41**	4.9
		(−.13;.39)	(.07;.55)	(−.13;.39)	(−.13;.42)	(−.38;.14)	(−.55;-.07)	(−.24;.29)	(.05;.54)	(−.59;-.12)	
	5.0	08	38**	17	32	-.16	-.29	11	28	-.44**	8.6**
		(−.22;.32)	(.09;.57)	(−.15;.38)	(.05;.56)	(−.4;.13)	(−.55;-.06)	(−.17;.36)	(.08;.56)	(−.61;-.15	
	6.6	06	35**	19	29	-.19	-.25	03	29	-.46**	7.3**
		(−.24;.3)	(.07;.55)	(−.12;.41)	(.01;.53)	(−.4;.13)	(−.53;-.04)	(−.25;.29)	(.09;.57)	(−.63;-.18	
TMT-A (secs) (n = 56)	2.3	36**	−.40**	−.11	−.06	39**	52**	−.09	−.45**	58**	10.0**
TMT-B (secs) (n = 54)		(.1;.57)	(−0.58;-.12	(−.33;.19)	(−.27;.29)	(.18;.62)	(.24;.66)	(.47;.02)	(−.67;-.27)	(.34;.71)	
TMT interference time (secs) (n = 54)	1.4	.22	-.55**	-.24	-.22	.42**	38**	-.04	-.41**	68**	3.6
		(.06;.54)	(−0.7;-0.31)	(−.37;.16)	(−.47;.08)	(.18;.62)	(.14;.6)	(−.32;.22)	(−.63;-.18)	(.25;.67)	
	1.7	13	-.49**	-.25	-.27	32	23	-.01	-.35	62*	1.2
		(−.05;.46)	(−.68;-.27)	(−.35;.18)	(−.51;.02)	(.08;.56)	(.01;.51)	(−.3;.24)	(−.58;-.12)	(.12;.59)	
Modified SET rank score(n = 34)	11.4**	.28	.15	−.01	−.16	.12	−.08	.20	−.14	−.38	0.2
		(−.06;.57)	(−.12;.52)	(−.27;.4)	(−.44;.26)	(−.2;.46)	(−.43;.23)	(−.19;.48)	(−.32 ;.36)	(−.62;-.02)	
Questionnaires											
DEX-patient (n = 76)	4.4	−.03	−.25	−.11	−.08	.71**	.41**	−.33**	−.44**	.33**	12.8**
DEX-relative (n = 47)		(−.19;.26)	(−.38;.06)	(−.28;.17)	(−.23;.25)	(.55;.79)	(.17;.56)	(−.44;-.02)	(−.52;-.12)	(.11;.52)	
DEX-difference (n = 41)	0.9	.06	-.27	-.07	-.35	.08	.32	-.05	-.49**	.47**	6.6
		(−.27;.3)	(−.55;-02)	(−.34;.24)	(−.5;.1)	(−.31;.31)	(−.12;.46)	(−.35;.26)	(−.63;-.16)	(.16;.64)	
	2.6	14	-.04	06	-.34	-.51**	02	10	-.17	.14	0.1
		(−.33;.29)	(−.42;.19)	(−.24;.38)	(−.58 ;.02)	(−.7;-.23)	(−.37;.24)	(−.22;.39)	(−.4;.2)	(−0.34;.27)	
BICoQ-patient (n = 76)	2.3	−.01	−.29	−.09	−.09	67**	39**	−.52**	−.43**	44**	15.3**
BICoQ-relative (n = 48)		(−.2;.25)	(−.46;-.04)	(−.29 ;.17)	(−.31;.17)	(.55;.79)	(.2 ;.58)	(−.66;-.32)	(−.59 ;-.22)	(.22;.59)	
BICoQ-difference (n = 41)	0.2	13	-.26	-.35	-.26	21	28	-.23	-.61**	57**	15.6**
		(−.17;.39)	(−.48;.07)	(−.57;.05)	(−.54;.03)	(−.1;.49)	(.06;.59)	(−.48;.11)	(−.74;-0.35)	(.39;.76)	
	2.6	07	-.09	-.21	-.17	-.44**	-.08	31	-.24	25	0.5
		(−.24;.37)	(−.4;.21)	(−.48;.11)	(−.5;.13)	(−.67;-.18)	(−.33;.29)	(−.03;.54)	(−.48;.11)	(−.13;.47)	

PSI = processing speed index (standard score from the WAIS-IV); CVLT = California Verbal Learning Test; TMT = Trail Making Test; SET = Six-element test; DEX = Dysexecutive Questionnaire; BICoQ = Brain Injury Complaint Questionnaire; GCS = Glasgow Coma Scale; HADS = Hospital Anxiety and Depression Scale; FSS = Fatigue Severity Scale; QoL = Quality of Life; GOS-E = Glasgow Outcome Scale-extended; FI = Functional Independence; RTW = Return to Work; **: $p < .01$

Regarding Spearman correlation coefficients, the table presents the Rho (and 95% CI)

Table 4. Correlation analyses (Spearman's Rho (and 95% CI)). Relationships between neuropsychological testing and subjective questionnaires.

	DEX-P	DEX-R	DEX-D	BICoQ-P	BICoQ-R	BICoQ-D
Neuropsychological testing						
PSI (n = 53)	−.23	−.29	−.16	−.37**	−.18	−.05
	(−0.51;-.01)	(−.51;.16)	(−.38;.3)	(−0.6;-.14)	(−.6;.02)	(−.35;.34)
CVLT-first list total standard score (n = 54)	−.31	−.22	.11	−.38**	−.27	−.01
CVLT-short term free recall (n = 54)	(−.57;-.1)	(−.38;.29)	(−.15;.5)	(−.61;−.16)	(−.59;.01)	(−.24;.42)
CVLT- short term cued recall (n = 54)	-.26	-.34	-.17	-.42**	-.13	.01
CVLT- long term free recall (n = 53)	(−.48;.03)	(−.45;.2)	(−.36;.31)	(−.6;-.14)	(−.46;.19)	(−.22;.44)
CVLT- long term cued recall	-.19	-.27	-.05	-.34	-.15	.01
	(−.45;.06)	(−.38;.28)	(−.27;.39)	(−.53;-.04)	(−.48;.17)	(−.22 .44)
	-.17	-.34	-.22	-.35**	-.27	-.14
	(−.42;.11)	(−.49;.17)	(−.42;.25)	(−.57;-.09)	(−.56;.07)	(−.36;.32)
	-.17	-.30	-.11	-.35**	-.18	-.02
	(−.42;.11)	(−.43;.24)	(−.33;.34)	(−.54;-.05)	(−.53;.11)	(−.29;.39)
TMT-A (secs) (n = 56)	29	20	11	42**	26	07
TMT-B (secs) (n = 54)	(.15;.6)	(−.22;.43)	(−.37;.29)	(.27;.67)	(.0;.6)	(−.32;.34)
TMT interference time (secs) (n = 54)	.37**	.23	.01	.42**	.26	.04
	(.03;.53)	(−.26;.41)	(−.37;.3)	(.1;.57)	(.12;.52)	(−.37;.31)
	33	22	03	30	20	04
	(−.04;.47)	(−.27;.4)	(−.34;.34)	(.01;.51)	(−.19;.47)	(−.37;.3)
Modified SET rank score(n = 34)	−.02	−.11	−.12	−.09	−.01	.12
	(−.35;.33)	(−.49;.42)	(−.49;.42)	(−.44;.23)	(−.48;.43)	(−.4;.51)

DEX = Dysexecutive Questionnaire; BICoQ = Brain Injury Complaint Questionnaire; for both questionnaires: *P* = Patient scoring; R = Relative scoring; D = Difference score; PSI = processing speed index (standard score from the WAIS-IV); CVLT = California Verbal Learning Test; TMT = Trail Making Test; SET = Six-element test.
**: $p < .01$.

did not however significantly correlate with the Modified Six-Element test, nor with cognitive and complaint questionnaires.

Relationships between neuropsychological measures (tests and questionnaires) and injury severity

There was no statistically significant correlation between cognitive measures (tests or questionnaires) and injury severity variables (Table 3), although there was a trend for a few non-significant relationships ($p < .05$) with the GCS or post ICU-GOS. Correlation coefficients with coma duration are not shown on the table for clarity of presentation, as they were all far from significance (all Rhos <0.18).

Relationships between neuropsychological measures (tests and questionnaires) and mood, fatigue and life satisfaction

As can be seen in Table 3, statistically significant correlations were found between mood, as assessed with the total HADS score and speed of processing (time of completion of TMT-A and B), DEX-patient, DEX-difference, BICoQ-patient and BICoQ-difference. Fatigue was also significantly correlated with time of completion of the TMT and with both DEX-patient and BICoQ-patient, and in addition it was also significantly correlated with two verbal memory measures; fatigue was however not significantly related to DEX- and BICoQ- relative- nor -difference scores. Quality of life did not significantly correlate with any neuropsychological testing score, but was significantly correlated with patient's ratings of both the DEX and the BICoQ (but not with relative's ratings nor with difference scores).

Relationships between neuropsychological measures (tests and questionnaires) and functional outcome

Statistically significant correlations were found between the GOS-E score and the following cognitive measures (Table 3): time of completion of TMT-A and B, DEX-patient, DEX-relative, BICoQ-patient, and BICoQ-relative. Although there was a trend for significant correlations between the GOS-E and memory scores, these did not reach statistical significance after correction for multiple comparisons.

Regarding the functional independence questionnaire, statistically significant correlations were found with most neuropsychological testing scores with the exception of the Modified Six-Element test (PSI, CVLT cued- long-term recall, time of completion of TMT-A and B, TMT interference time), and with DEX-patient, DEX-relative, BICoQ-patient, and BICoQ-relative ratings.

Finally, return to work was statistically significantly related to the following measures: three out of five verbal memory scores, time of completion of TMT-A, DEX-patient, BICoQ-patient and BICoQ-relative.

Relationships between performance-based measures and questionnaires

As can be seen on Table 4, there were only poor relationships between neuropsychological testing and the DEX. The only significant correlation concerned the DEX-patient and TMT-B (although there was a non-significant trend for a few other correlations). Regarding the BICoQ, the patients' ratings were significantly related to verbal memory and speed of processing (PSI and TMT A and B). There was no significant correlation between neuropsychological testing and relatives' scores nor with difference scores.

Regression analyses

A linear regression analysis was computed to assess the independent effect of cognition on functional outcome. The GOS-E score was used as dependent variable. Three blocks of independent variables were successively entered into the regression equation. The first block included demographic variables (age and education duration), the second block included injury severity measures (GCS, coma duration and GOS score upon ICU discharge), and the third block included a selection of cognitive measures which were found significantly correlated with the GOS-E in univariate analyses (TMT-A and DEX-patient score). The BICoQ was not included in the model, as it appeared highly correlated with the DEX. The model was found statistically significant (F (7,34) = 6.24, $p > .001$) and reliable (Durbin–Watson statistics = 2.23). The R square was .34 for the first block of independent variable (demographics, $p < .001$, standardized Beta coefficients = −.31 for age and .58 for education duration). Block 2 (injury severity) did not significantly improve the model (R square change = .04, $p > .1$, standardized Beta coefficients = −.31 for age, .54 for education duration, and ranging from −.01 to .13 for injury severity measures), however, block 3 did significantly improve the model (R square change = .18, $p < .01$). Overall, the third model explained 56.2% of the total GOS-E variance. Only education duration and TMT-A were significantly independently related to GOS-E (standardized Beta coefficients = .33 and −.41 respectively, $p < .05$), all other variables did not reach statistical significance (standardized Beta coefficients ranging from .11 to .18).

Considering the significant effect of education duration on outcome, to rule out any possible confounding effect of this variable, which was also found to be associated to loss to follow-up, additional analyses were computed to assess the clinical significance of neuropsychological measures after controlling for education. For this purpose, patients were divided in two groups based on their GOS-E score (unfavorable outcome = Severe and lower Moderate Disability; favorable outcome = upper Moderate Disability and Good Recovery). Separate one-way analyses of covariance (ANCOVAs) were computed for each of the neuropsychological outcome measures with group (favorable vs unfavorable) as between-subject variable, and education duration as covariate. Only three of these analyses showed a significant effect of group, due to more severe impairments in the unfavorable outcome group after control for education duration: TMT-A (favorable group: mean = 38.9 SD = 18.2 secs; unfavorable group: mean = 61.0 SD = 32.8 secs; F (,53) = 5.7, $p = .02$); DEX-relative (favorable group: mean = 18.5 SD = 31.7; unfavorable group: mean = 31.7 SD = 16.6; F (2,34,) = 5.6, $p = .02$) and BICOQ-relative (favorable group: mean = 11.07 SD = 6.0; unfavorable group: mean = 16.6 SD = 4.8; F (2,34,) = 7.6, $p = .008$). All other group comparisons were not significant ($p > .05$).

Discussion

The objective of the present study was to assess the relationships between neuropsychological impairments and different dimensions of outcome in a homogenous prospective sample of patients with severe TBI at a chronic stage (8 years post injury). The term neuropsychological impairments was used here as an umbrella term including different domains, such as deficits in cognitive functions (memory, attention, executive functions and speed of processing), but also behavioral and personality changes which are commonly encountered in patients with severe TBI. Cognitive impairments (measured by tests) and behavioral changes (measured by self- or proxy-rated questionnaires) are frequently associated but they may also dissociate, the most frequent type of dissociation being (sub)normal performance on tests contrasting with behavioral changes according to relatives (34). Accordingly, two sets of measures of neuropsychological outcome were taken: performance-based measures, including common neuropsychological tests; and patient or relative-based measures, including questionnaires focusing on the subjective impact of such deficits in everyday life, both from the patient's and a close relative's perspective (the DEX (30) and the BICoQ (32)). Raw scores were used for most cognitive test scores, except for the PSI and the CVLT-first list total standard scores. However, the effects of age and education were controlled for in the regression model. Different outcome measures were obtained, including measures of mood, fatigue, satisfaction with life, and functional outcome (GOS-E, a functional independence score designed specifically for this study and employment).

Although gender only had a marginal effect on cognitive outcome, age and education had significant effects on speed of processing, but only education duration was significantly related to verbal memory. These findings are in accordance with previous research showing the negative effect of age and the positive effect of education on neuropsychological outcome (17,20,34,35).

Interestingly, no initial injury severity measure (GCS, coma duration and disability upon ICU discharge) significantly correlated with neuropsychological outcome. The GOS at discharge from ICU is a relatively crude measure of outcome, but it is difficult at this stage to obtain more reliable measurements of the patient global level of functioning. Unfortunately, post-traumatic amnesia, which has been found to be a better predictive measure of outcome, could not been used in the present study, due to a high number of missing values. Nevertheless, these findings are not really surprising, as the limited value of injury severity measures in predicting long-term outcome, at least in samples including only patients with severe TBI, has been reported in previous research (11,12,35). It should be outlined that, in a previous study on the same sample, we found a weak but significant correlation between injury severity and disability, as assessed with the GOS-E (19). However, cognition is determined by a complex combination of factors, such as cognitive reserve, mood, social environment, which may explain the lack of significant relationship with injury severity. These different findings therefore suggest that initial injury severity measures poorly predict long-term neuropsychological outcome, particularly in samples limited to patients with severe injuries, such as the present one. Different findings should be expected in samples including a wider range of injury severity (i.e. patients with mild and moderate TBI).

We investigated the relationships between neuropsychological impairments and selected subjective measures of outcome, including mood, fatigue and satisfaction with life. The main findings were that neuropsychological tests (mainly mental speed) were marginally correlated with mood and fatigue, but were not significantly related to quality of life. By contrast, patients' ratings of the DEX and the BICoQ were significantly related with mood, fatigue and quality of life. These findings are in accordance with current theoretical accounts according to which mental fatigue results from the efforts required to overcome the effect of slowed processing to meet everyday life demands (36,37). They are also in accordance with previous findings suggesting that quality of life is a complex and multi-determined issue (17,38,39,40) which cannot be captured with examiner's-based measures. For example, Williams et al. (8) found that the Satisfaction With Life Scale score was not significantly predicted by a combination of injury-related, CT characteristics and cognitive factors. Due to time limits in the follow-up assessments, we did not use in the present study a well-validated scale such as the QOLIBRI (40) which was used at 4-year follow-up (17). This may represent a limitation to the study. Nevertheless, the finding of significant correlations with other subjective measures (DEX and BICOQ) contrasting with the lack of significant correlation with neuropsychological testing suggests at least some degree of validity of the visual-analog scale of life satisfaction which was used here.

Regarding functional outcome and disability, the functional independence score, the GOS-E, and employment outcome appeared to be significantly related with several cognitive testing scores, and with the DEX and the BICoQ (patient and relative ratings). The strength of correlations fell in the moderate range (0.4 to 0.6). These findings are globally in accordance with previous studies on cognitive predictors of return to work (34,41,42) and with the Allanson et al. (13) meta-analysis and suggest that neuropsychological tests, particularly of speed of processing and verbal memory, are quite strong predictors of functional outcome, whatever the measure chosen. In addition, the current findings also suggest that cognitive questionnaires either rated by the patient himself and/or by a close relative, also significantly predict functional outcome, thus raising questions regarding the assumption that patients with severe TBI lack awareness of their persisting impairments. Actually, the present results suggest that, at least in the long-term, many years after the injury, patient's subjective accounts are not so far from their actual level of functioning. Accordingly, in a previous study with the same cohort at an earlier (4-year) stage, we found only relatively small (although statistically significant) differences between patient's and relative's scores on the BICoQ (32,43).

Additionally, we tested the relationships between neuropsychological tests and self or proxy-rated questionnaires. While there was only little significant correlation between the DEX-patient and speed of processing, the BICoQ-patient score appeared well correlated with many neuropsychological scores (verbal memory and speed of processing). The relationships between the DEX and neuropsychological measures have been a matter of debate in the literature, with some studies reporting positive findings, while others did not (44–4748). The present study suggests that there seems to be quite little relationships between the DEX and formal testing. This issue had not been tested previously with the BICoQ, and the present results suggest that this complaint questionnaire is relatively well related to cognitive testing. Again here, patient's scores surprisingly appeared to be a stronger predictor of outcome than relative's scores.

Finally, the regression analysis showed that cognition had a significant impact on functional outcome, above and beyond the effect of demographic variables such as age and education, and injury severity measures. Indeed, inclusion of the TMT-A and of the DEX significantly increased the predictive value of the model. It appeared that the TMT-A, which is a simple measure of speed of processing, was the best single predictor of functional outcome, in addition to education duration, which is in accordance with previous research, which also showed the profound effect of slowed information processing on outcome after severe TBI. Influence of other factors, such as genetic factors (APOE status) could not unfortunately be tested in the present study. Moreover, we conducted additional analyses to compare patients with favorable outcome (upper Moderate Disability and Good Recovery) with those with unfavorable outcome (Severe and lower Moderate Disability) after statistically controlling for education duration. Three measures were found to be associated with significantly poorer scores in the unfavorable group after control for education: the TMT-A, and DEX- and BICOQ-relative scores. This again suggests that these measures are the strongest predictors of global disability.

The main limitation of this study is the relatively small sample size, due to a high attrition rate. The attrition rate is an important concern in all long-term longitudinal studies such as the present one, and may be a source of bias. We had previously addressed this issue in the whole PariS-TBI cohort at different time points (1-, 4-, and 8-year post injury, attrition rate being respectively 47%, 40% and 63.5%) (19,50). The main reason for loss to follow-up was impossibility to achieve contact due to erroneous or changed address, e-mail, and/or phone number (respectively 42.4%, 20.2% and 54.2% of survivors at each time point). Refusal to participate was very are at 1-year (4.2% of survivors) but more frequent at 4- (14.7%) and 8-year (9.3%). Other anecdotal causes (such as patients moving abroad) were rare. Patients lost to follow-up were compared to included patients on a wide range of measures. The two groups did not significantly differ in terms of injury severity, age nor gender. The trauma mechanism had a significant effect at 1-year follow-up (non-accidental fall or aggression were more often associated with loss to follow-up), although this was not significant at later assessments. A poorer social and educational status (unemployment before the accident, lower vocational level, or shorter education duration) appeared to be the most robust predictor of loss to follow-up, at each of the three time points. In accordance with these previous findings, patients included in the present study did not significantly differ from lost-to-follow up patients in terms of injury severity, although there were significant differences regarding education and pre-injury employment. To minimize the risk of bias in statistical analyses, we included education duration in the regression model to assess the independent effect of cognition on functional outcome.

However, the relatively small sample size raises concerns regarding non-significant comparisons, which could indeed be due to a lack of statistical power, particularly after statistical correction for multiple comparisons, which led us to consider as significant only results with a p value lower than .01. It was not possible, for clarity of presentation, to show all p values in the tables presented here. However, the correlation coefficients (with 95%CI) provide a clear representation of the effect-size of the relationships between the different variables, and hence of their clinical, not only statistical, significance.

The threshold for statistical significance here was a Spearman's Rho above 0.30, corresponding to a moderate effect-size. Correlations below such threshold, even if they would have reached statistical significance with a larger sample size, would nevertheless be of questionable clinical significance.

To conclude, this long-term follow-up study showed that, at least up to eight years post trauma, neuropsychological measures, particularly slowed information processing speed, are significant indicators of functional outcome in patients with severe TBI, while injury severity measures appeared to be poorly related to outcome at this stage.

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The authors have no conflict of interest to disclose.

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Author contributions

CVA, AR, EB, PPD, JC, CJ and PAz contributed to the study design and monitoring.

CVA, GN and MS contributed to data collection, data clearing and statistical analyses.

IG, LM and PAe contributed to data management, statistical supervision, and administrative and financial matters.

CVA, PAz, AR and CJ contributed to writing the manuscript.

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References

1. Azouvi P, Arnould A, Dromer E, Vallat-Azouvi C. Neuropsychology of traumatic brain injury: an expert overview. Rev Neurol (Paris). août. 2017;173(7-8):461-72. doi:10.1016/j.neurol.2017.07.006.
2. Maas AIR, Menon DK, Adelson PD, Andelic N, Bell MJ, Belli A, Bragge P, Brazinova A, Büki A, Chesnut RM, et al. Traumatic brain injury: integrated approaches to improve prevention, clinical care, and research. Lancet Neurol. Déc. 2017;16(12):987-1048.
3. Forslund MV, Perrin PB, Røe C, Sigurdardottir S, Hellstrøm T, Berntsen SA, Lu J, Arango-Lasprilla JC, Andelic N. global outcome trajectories up to 10 years after moderate to severe traumatic brain injury. Front Neurol. 2019;10:219.
4. Jourdan C, Bayen E, Vallat-Azouvi C, Ghout I, Darnoux E, Azerad S,Charanton J, Aegerter P, Pradat-Diehl P, Ruet A. Late functional changes post-severe traumatic brain injury are related to community reentry support: Results from the PariS-TBI cohort. J Head Trauma Rehabil. janv. 2017;5.
5. Ruet A, Bayen E, Jourdan C, Vallat-Azouvi C, Azerad S, Grimaldi Meaude L, Charanton J, Azouvi P. Potential for recovery between 4 and 8 years after a severe traumatic brain injury. Data from the PariS-TBI longitudinal study. Ann Phys Rehabil Med août. 2021 Mar; 64 (2): 101422.
6. Sigurdardottir S, Andelic N, Røe C, Schanke A-K.Trajectory of 10-year neurocognitive functioning after moderate-severe traumatic brain injury: early associations and clinical application. J Int Neuropsychol Soc JINS. août. 2020;26 (7):654-67.
7. Ponsford J, Harrison-Felix C, Ketchum JM, Spitz G, Miller AC, Corrigan JD. Outcomes 1 and 2 years after moderate to severe traumatic brain injury: an international comparative study. Arch Phys Med Rehabil. 2021 Mar; 102 (3): 371-377.
8. Williams MW, Rapport LJ, Hanks RA, Millis SR, Greene HA. Incremental validity of neuropsychological evaluations to computed tomography in predicting long-term outcomes after traumatic brain injury. Clin Neuropsychol. 2013;27(3):356-75. doi:10.1080/13854046.2013.765507.
9. Hanks RA, Jackson AM, Crisanti LK. Predictive validity of a brief outpatient neuropsychological battery in individuals 1-25 years post traumatic brain injury. Clin Neuropsychol. 2016 oct;30 (7):1074-86. doi:10.1080/13854046.2016.1194479.
10. Bercaw EL, Hanks RA, Millis SR, Gola TJ. Changes in neuropsychological performance after traumatic brain injury from inpatient rehabilitation to 1-year follow-up in predicting 2-year functional outcomes. Clin Neuropsychol. janv. 2011;25(1):72-89. doi:10.1080/13854046.2010.532813.
11. Ponsford J, Draper K, Schonberger M. Functional outcome 10 years after traumatic brain injury: its relationship with demographic, injury severity, and cognitive and emotional status. J Int Neuropsychol Soc. mars. 2008;14(2):233-42. doi:10.1017/S1355617708080272.
12. Wood RL, Rutterford NA. Demographic and cognitive predictors of long-term psychosocial outcome following traumatic brain injury. J Int Neuropsychol Soc JINS. mai. 2006;12(3):350-8. doi:10.1017/S1355617706060498.
13. Allanson F, Pestell C, Gignac GE, Yeo YX, Weinborn M. Neuropsychological predictors of outcome following traumatic brain injury in adults: a meta-analysis. Neuropsychol Rev. 2017 sept;27(3):187-201. doi:10.1007/s11065-017-9353-5.
14. Wilson L, Horton L, Kunzmann K, Sahakian BJ, Newcombe VF, Stamatakis EA,von Steinbuechel N, Cunitz K, Covic A, Maas A. Understanding the relationship between cognitive performance and function in daily life after traumatic brain injury. J Neurol Neurosurg Psychiatry. 2020;2.
15. Wilson JT, Pettigrew LE, Teasdale GM.Structured interviews for the glasgow outcome scale and the extended glasgow outcome scale: guidelines for their use. J Neurotrauma. Août. 1998;15 (8):573-85.
16. Rappaport M, Hall KM, Hopkins K, Belleza T, Cope DN.Disability rating scale for severe head trauma: Coma to community. Arch Phys Med Rehabil. 1982;63(3):118-23.
17. Azouvi P, Ghout I, Bayen E, Darnoux E, Azerad S, Ruet A, Vallat-Azouvi C, Pradat-Diehl P, Aegerter P, Charanton J. Disability and

health-related quality-of-life 4 years after a severe traumatic brain injury: a structural equation modelling analysis. Brain Inj. 2016;30 (13-14):1665-71. doi:10.1080/02699052.2016.1201593.
18. Jourdan C, Bayen E, Pradat-Diehl P, Ghout I, Darnoux E, Azerad S, Vallat-Azouvi C, Charanton J, Aegerter P, Ruet A. A comprehensive picture of 4-year outcome of severe brain injuries. Results from the PariS-TBI study. Ann Phys Rehabil Med. avr. 2016;59(2):100-6. doi:10.1016/j.rehab.2015.10.009.
19. Ruet A, Bayen E, Jourdan C, Ghout I, Meaude L, Lalanne A, Pradat-Diehl P, Nelson G, Charanton J, Aegerter P. A detailed overview of long-term outcomes in severe traumatic brain injury eight years post-injury. Front Neurol. 2019;10:120.
20. Jourdan C, Bosserelle V, Azerad S, Ghout I, Bayen E, Aegerter P, Weiss JJ, Mateo J, Lescot T, Vigué B. Predictive factors for 1-year outcome of a cohort of patients with severe traumatic brain injury (TBI): results from the PariS-TBI study. Brain Inj. 2013;27 (9):1000-7. doi:10.3109/02699052.2013.794971.
21. Jennett B, Bond M.Assessment of outcome after severe brain damage. Lancet. 1975;1(7905):480–84.doi:10.1016/S0140-6736(75) 92830-5.
22. Maas AIR, Harrison-Felix CL, Menon D, Adelson PD, Balkin T, Bullock R, Engel DC, Gordon W, Langlois-Orman J, Lew HL. Standardizing data collection in traumatic brain injury. J Neurotrauma. Févr. 2011;28(2):177-87.
23. Truelle JL, Van Zomeren AD, De Barsy T, Brooks DN, Janzik HH, Lay WA. European head injury evaluation chart. Scand J Rehabil Med Suppl. 1992;26:115-25.
24. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand. juin. 1983;67(6):361-70. doi:10.1111/j.1600-0447.1983.tb09716.x.
25. Krupp LB, LaRocca NG, Muir-Nash J, Steinberg AD. The fatigue severity scale. Application to patients with multiple sclerosis and systemic lupus erythematosus. Arch Neurol. 1989 oct;46(10):1121-3. doi:10.1001/archneur.1989.00520460115022.
26. Wechsler D. WAIS-IV. Paris: Edition du Centre de Psychologie Appliquée; 2011.
27. Delis DC, Kramer JH, Kaplan E, Ober B. The california verbal learning test: Research edition. New York: Psychological Corporation; 1987.
28. Godefroy O, Azouvi P, Robert P, Roussel M, LeGall D, Meulemans T, et al. Dysexecutive syndrome: diagnostic criteria and validation study. Ann Neurol. déc. 2010;68(6):855-64. doi:10.1002/ana.22117.
29. Reitan RM.Validity of the trail making test as an indicator of organic brain damage. Percept Mot Skills. 1958;8(3):271-6. doi:10.2466/pms.1958.8.3.271.
30. Burgess PW, Alderman N, Evans J, Emslie H, Wilson B.The ecological validity of tests of executive function. J Int Neuropsychol Soc. 1998;4(6):547-58.doi:10.1017/S1355617798466037.
31. Azouvi P, Vallat-Azouvi C, Millox V, Darnoux E, Ghout I, Azerad S, Ruet A, Bayen E, Pradat-Diehl P, Aegerter P. Ecological validity of the Dysexecutive Questionnaire: results from the PariS-TBI study. Neuropsychol Rehabil. 2015;25 (6):864-78. doi:10.1080/09602011.2014.990907.
32. Vallat-Azouvi C, Paillat C, Bercovici S, Morin B, Paquereau J, Charanton J, Ghout I, Azouvi P. Subjective complaints after acquired brain injury: presentation of the Brain Injury Complaint Questionnaire (BICoQ). J Neurosci Res. avr. 2018;96(4):601-11. doi:10.1002/jnr.24180.
33. Chesnel C, Jourdan C, Bayen E, Ghout I, Darnoux E, Azerad S, Charanton J, Aegerter P, Pradat-Diehl P, Ruet A. Self-awareness four years after severe traumatic brain injury: discordance between the patient's and relative's complaints. Results from the PariS-TBI study. Clin Rehabil. mai. 2018;32(5):692-704. doi:10.1177/0269215517734294.
34. Cappa KA, Conger JC, Conger AJ.Injury severity and outcome: a meta-analysis of prospective studies on TBI outcome. Health Psychol. Sept. 2011;30(5):542-60.
35. Willemse-van Son AHP, Ribbers GM, Verhagen AP, Stam HJ. Prognostic factors of long-term functioning and productivity after traumatic brain injury: a systematic review of prospective cohort studies. Clin Rehabil. 2007 nov;21(11):1024-37. doi:10.1177/0269215507077603.
36. Belmont A, Agar N, Azouvi P. Subjective fatigue, mental effort, and attention deficits after severe traumatic brain injury. Neurorehabil Neural Repair. 2009 nov;23(9):939-44. doi:10.1177/1545968309340327.
37. Ziino C, Ponsford J. Selective attention deficits and subjective fatigue following traumatic brain injury. Neuropsychology. mai. 2006;20(3):383-90. doi:10.1037/0894-4105.20.3.383.
38. Mailhan L, Azouvi P, Dazord A. Life satisfaction and disability after severe traumatic brain injury. Brain Inj. avr. 2005;19 (4):227-38. doi:10.1080/02699050410001720149.
39. Bullinger M, Azouvi P, Brooks N, Basso A, Christensen A-L, Gobiet W, Greenwood R, Hütter B, Jennett B, Maas A. Quality of life in patients with traumatic brain injury-basic issues, assessment and recommendations. Restor Neurol Neurosci. 2002;20 (3-4):111-24.
40. Von Steinbüchel N, Wilson L, Gibbons H, Hawthorne G, Höfer S, Schmidt S, Bullinger M, Maas A, Neugebauer E, Powell J. Quality of life after brain injury (QOLIBRI): scale validity and correlates of quality of life. J Neurotrauma. juill. 2010;27(7):1157-65.
41. Benedictus MR, Spikman JM. van der Naalt J. Cognitive and behavioral impairment in traumatic brain injury related to outcome and return to work. Arch Phys Med Rehabil. 2010 sept;91 (9):1436-41. doi:10.1016/j.apmr.2010.06.019.
42. Sawamura D, Ikoma K, Ogawa K, Sakai S. Clinical utility of neuropsychological tests for employment outcomes in persons with cognitive impairment after moderate to severe traumatic brain injury. Brain Inj. 2018;23:1-8.
43. Chesnel C, Jourdan C, Bayen E, Ghout I, Darnoux E, Azerad S, et al. Self-awareness four years after severe traumatic brain injury: discordance between the patient's and relative's complaints. Results from the PariS-TBI study. Clin Rehabil. 2017 oct;1:269215517734294.
44. Azouvi P, Vallat-Azouvi C, Millox V, Darnoux E, Ghout I, Azerad S, et al. Ecological validity of the Dysexecutive Questionnaire: results from the PariS-TBI study. Neuropsychol Rehabil. déc. 2014;18:1-15.
45. Bennett PC, Ong B, Ponsford J.Measuring executive dysfunction in an acute rehabilitation setting: using the dysexecutive questionnaire (DEX). J Int Neuropsychol Soc. Juill. 2005;11(4):376-85.
46. Boelen DH, Spikman JM, Rietveld AC, Fasotti L. Executive dysfunction in chronic brain-injured patients: assessment in outpatient rehabilitation. Neuropsychol Rehabil. 2009 oct;19(5):625-44. doi:10.1080/09602010802613853.
47. Norris G, Tate RL.The behavioural assessment of the dysexecutive syndrome: Ecological, concurrent and construct validity. Neuropsychol Rehabil. 2000;10(1):33-45.doi:10.1080/096020100389282.
48. Jourdan C, Bayen E, Bahrami S, Ghout I, Darnoux E, Azerad S, Ruet A, Vallat-Azouvi C, Weiss JJ, Aegerter P. Loss to follow-up and social background in an inception cohort of patients with severe traumatic brain injury: Results from the PariS-TBI study. J Head Trauma Rehabil. 2015;19.