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Functional status 1 year after severe childhood traumatic brain injury predicts 7-year outcome: results of the TGE study

Running head: Functional impairments 1-year after severe childhood TBI predict long-term outcome

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Functional status 1 year after severe childhood traumatic brain injury predicts 7-year outcome: results of the TGE study

Abstract

Background. Childhood severe traumatic brain injury (TBI) is a leading cause of long-lasting acquired disability, but predicting long-term functional outcome remains difficult.

Objectives. This study aimed to 1) describe the functional outcome at 1 and 7 years post-TBI; 2) determine the initial and concurrent factors associated with long-term outcome; and 3) evaluate the predictive value of functional status, overall disability level and intellectual ability measured at 1 year post-injury to determine 7-year clinically meaningful outcomes.

Methods. Among the children (<16 years) consecutively included over 3 years in the *Traumatisme Grave de l'Enfant* (TGE) prospective longitudinal cohort study after accidental severe TBI, we studied the outcomes of 39 survivors at 1 and 7 years post-injury. Overall outcome included disability level (Glasgow Outcome Scale), functional status (Pediatric Injury Functional Outcome Scale), intellectual ability (Wechsler scales), executive functions (Behavior Rating Inventory of Executive Functions), behaviour (Child Behavior Checklist) as well as neurological impairments and academic status.

Results. Mean (SD) age of the 39 survivors at injury was 7.6 (4.6) years, and long-term evaluation was conducted at a mean of 7.8 years post-injury (range 5.9–9.3); 36% of participants were adults (≥ 18 years old). Most of the neurological impairments remained stable beyond 1 year after TBI, whereas overall disability level improved significantly from 1 to 7 years but remained highly variable, with almost half of participants presenting significant disability levels (moderate: 26%, or severe: 21%). Almost half of participants had significant cognitive, behaviour and/or academic difficulties at 7 years post-TBI. On multivariate regression analysis, functional impairment at 1 year was the best predictor of severe disability at 7 years ($F_{(3,31)}=13.18$, $p<0.001$, sensitivity=100%, specificity=78%).

Conclusions. Our results confirm the significant long-term impact of childhood severe TBI. All children with TBI should benefit from systematic follow-up, especially those with persistent functional

deficits at 1 year post-injury, because the severity of functional impairment at 1 year seems the best predictor of long-term significant disability up to 7 years post-TBI.

Keywords: severe traumatic brain injury; child; functional outcome; disability; longitudinal cohort study; long-term follow-up

Introduction

Childhood traumatic brain injury (TBI) remains a leading cause of mortality and acquired long-term disability worldwide [1,2]. Children with severe TBI, defined by Glasgow Coma Scale (GCS) score ≤ 8 [3], present worse long-term outcomes as compared with mild TBI [4,5], but predicting long-term outcomes at the early phase is difficult.

Because severe childhood TBI occurs in a developing brain, it can disrupt subsequent neurodevelopment, causing significant long-lasting alterations in a wide range of functional abilities [2,4,6,7]. Importantly, these disabling impairments might not be realized until years post-injury, when higher-level cognitive and behaviour functioning is required to meet typical developmental milestones [2,6,8,9]. Failure to meet these milestones affects the child's daily activities and school functioning [10,11], with consequences for later social integration and participation [2,12,13]. Overall, cognitive, behaviour and socio-emotional impairments are highly prevalent several years after severe TBI [7,14–16].

During the initial stage of rehabilitation care (i.e., in the first months after intensive care unit [ICU] discharge), the main medical challenge is to accurately assess the patient's impairments and functional state in order to adapt and personalize the initial therapeutic strategy. Subsequently, one must carefully follow the evolution of limitations in all functional areas and consider the patient's and family's complaints and requests, aiming to optimize the overall management during this recovery period. The assessment tools used throughout this process should be sensitive to change and take into account the need for complementary and ideally multimodal evaluations, but above all represent the patient's actual functional state. The Pediatric Injury Functional Outcome Scale (PIFOS) seems particularly

suitable for determining and monitoring functional impairment evolution and outcome of pediatric injury-specific sequelae [17] over the first years post-injury [18].

The clinical stabilization of functional outcomes is typically reached at about 1 year post-injury [14,18,19], after significant improvement from 1 month to 1 year after TBI, without further significant progress between 1 and 2 years after [18]. At this stage, the interventions aim at optimizing patients' capacities and autonomy while limiting the functional consequences of their impairments in order to improve long-term functional outcome, participation and quality of life. Therefore, early prognostic factors associated with recovery and later outcome are essential to identify the most vulnerable patients who would benefit from closer follow-up and tailored interventions aimed at improving their overall and functional outcome.

The *Traumatisme Grave de l'Enfant* (TGE) prospective longitudinal cohort study had the overall goal of assessing mortality and morbidity after severe pediatric TBI. This study involved serial assessments performed over the first 2 years post-injury and about 7 years post-TBI and evaluated the Full-Scale Intellectual Quotient (FSIQ), academic status, and overall disability (GOS), functional outcome (PIFOS), and included parent-rated questionnaires assessing executive functioning and behaviour.

The aims of this study were threefold: 1) to describe medium- and long-term functional outcome and overall level of disability at 1 and 7 years after severe childhood TBI; 2) to investigate initial and concurrent factors associated with outcome at 7 years post-injury (overall level of disability, intellectual functioning and academic status); and 3) to examine the predictive value of functional status, overall disability level and intellectual ability at 1 year post-injury on long-term clinically meaningful outcomes at 7 years. We hypothesized that the severity of functional impairment, overall disability level and intellectual ability at 1 year post-injury would be good predictors of long-term clinically meaningful outcomes, including the degree of disability.

The present report follows the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement.

Methods

Participants

From January 2005 to December 2008, 81 children (<16 years old) in the main Parisian pediatric neurosurgical ICU were included in the study within the first 6 hr after severe accidental TBI, defined as GCS score ≤ 8 and/or Injury Severity Score (ISS) >16 . Exclusion criteria were no vital signs upon admission or inflicted head injury. A total of 65 (80%) children survived and had systematic longitudinal follow-up over the first 2 years post-injury. In the present study, we focused on the 39 patients (60% of the survivors) who participated in both the 1-year and 7-year follow-up.

Measures

Sociodemographic background and pre-injury history. We collected data on sex, family background (marital status, family size, language spoken at home, parental education level), pre-injury academic status (grade delay) and significant medical history.

Initial injury severity. We used the lowest GCS score [3] measured within the first 24 hr, the initial ISS [20], the initial Pediatric Trauma Score (PTS) [21], and length of coma (in days) as quantitative markers of TBI severity.

Injury-related characteristics. We recorded age at injury and collected medical data during the acute ICU phase (e.g., presence of intracranial hypertension, penetrating skull fracture and acute neurosurgery required; see Table 1).

Outcome measures

The follow-up assessments performed at 1 and 7 years post-injury included a medical interview and neurological examination (e.g., presence of post-traumatic epilepsy, motor impairments, sensory deficits; Table 2), as well as a comprehensive neuropsychological assessment.

Overall level of disability. We used an adapted version of the GOS modified for children (GOS-Peds) [22] to assess overall disability at 1 year post-TBI into 5 categories (1, good recovery; 2, moderate disability; 3, severe disability; 4, vegetative state; 5, death). At 7 years post-injury, we used the GOS-Extended pediatric (GOS-E Peds) [23] and GOS-E adult version (GOS-E) [24]. The GOS-E adult

version yields categories ranging from 1 (dead) to 8 (good recovery, upper level), and the GOS-E Peds categories are organized in the opposite way (1, good recovery, upper level; 8, dead). We re-coded the results of the GOS-E to align them with the categories of the GOS-E Peds. To facilitate data comparisons between 1 and 7 years post-injury, the 7-year GOS-E/Peds results were collapsed into the 1-year GOS-Peds categories (hereafter named GOS-Peds*).

Functional outcome. We used the PIFOS [17], a brief injury-specific multidimensional rating scale for children aged 3 to 15 years, which was completed by a trained healthcare provider during a structured interview with parents at 1 year post-injury. This scale assessed performance in relation to pre-injury levels of functioning. We used the PIFOS version available at the time of the study that consisted of 26 items, rating 6 areas of function (motor, daily living, communication skills, social-emotional, cognition/academic functioning, and physical changes) on a 4-point Likert scale (0, no change from pre-injury levels; 2 to 4, increasing need for support and significant functional limitations). Higher PIFOS scores reflect greater difficulties (raw score range, 0-104). The last version (2014) evaluates the same 26 items but is grouped differently (academic item became the 7th sub-item) and the 0 rating became 1 (no change from pre-injury levels) in the 4-point rating. Thus, the interpretation of the total score was still unchanged, but absolute raw scores cannot be compared between versions (score range 26-104 in the last version). In this study, we focused on the total score and used the corresponding categorical scores ranging from 0 to 4 (0–1, absence or mild difficulties; 1–2, moderate impairment; 2–4, severe to very severe impairment) for the 32 participants with available PIFOS data at 1-year post-TBI. The PIFOS was not applicable at 7 years post-injury because of the intrinsic notion of comparing the current state with the pre-traumatic state.

Intellectual ability. We used age-appropriate French versions of the Wechsler Intelligence Scale [25–28] to assess FSIQ at both times.

Academic status. We recorded academic data at both times and classified ongoing education into 3 classes: mainstream school without or with any type of adaptation and/or grade retention, and special education.

Executive functioning was measured by using age-appropriate French adaptations of parent-reporting forms of the Behavior Rating Inventory of Executive Functions (BRIEF) [29] and its adult version (BRIEF-A) [30]. We used the Global Executive Composite score (GEC; *T*-score, mean [SD] 50 [10], clinical cut-off score ≥ 65), higher scores indicating worse executive functioning.

Behaviour. We used age-appropriate versions of the parent-reporting forms of Child Behavior Checklist (CBCL) [31] and its adult version (ABCL) [32]. We used the total behaviour problems *T*-score (mean 50 [SD], clinical cut-off score ≥ 65), higher scores indicating more behaviour problems.

Procedure

The TGE study was initiated in the Paris-5 University Hospital Necker-Enfants-Malades. Follow-up occurred in the Rehabilitation Department for Children with Acquired Neurological Injury at Saint Maurice Hospitals. The *Comité de Protection de Personnes d'Île-de-France VI* (CPP IDF-VI) ethics committee granted ethical approval to conduct this study. All parents and/or patients provided informed written consent.

Data analysis

Data analysis was performed with SAS 9. We used descriptive statistics to report sociodemographic and medical characteristics and the main outcomes at each time. We used univariate statistical analyses (Student *t* test, paired *t*-test, Pearson and Spearman correlation, chi-square or Fisher exact test, repeated measures ANOVA) and multivariate linear regressions (SAS GLM procedure) to examine the evolution of the main outcomes across times and the associations between the 1- and 7-year outcomes. Statistical significance was 2-tailed and was set at $p < 0.05$.

Results

Sociodemographic, pre-injury, severity and injury-related characteristics (Table 1)

Mean (SD) age at injury was 7.6 (4.6) years, and long-term evaluation was conducted at a mean of 7.8 years post-injury (range 5.9–9.3), with mean age 15.4 (4.4) years; 14 (36%) of participants were adults (≥ 18 years old). Participants followed at 7 years post-injury ($n=39$) and those who were lost to follow-

up ($n=26$) did not differ in sociodemographic characteristics or markers of initial injury severity (ISS, PTS, length of coma), except for GCS score, which was marginally significantly lower (higher severity) in the study group. We found no significant differences for any of the 1-year post-injury outcomes (PIFOS, GOS, FSIQ, BRIEF, CBCL).

Clinical impairments, medical management, and educational status at 1 and 7 years post-injury (Table 2)

Long-term neurological sequelae remained significant at 7 years post-TBI, with 10% of participants presenting post-traumatic epilepsy or hearing deficits and 18% visual impairments. Motor impairments improved slightly but not significantly (decreased) between 1 (36%) and 7 years (26%). At 7 years post-injury, almost 1 in 5 participants had undergone at least one surgery related to TBI sequelae.

Six (15%) participants were no longer in any educational program at 7 years (Fig. 1A): 5 were adults who had obtained a vocational diploma (high school or lower training grade), and the younger patient had socio-behaviour issues responsible for school failure and dropout (despite intellectual ability in the high average range). Among participants enrolled in an educational program, the proportion who required special education (including special education within rehabilitation centers for some still receiving hospital care at 1 year) was 31% at 1 year and 23% at 7 years post-TBI. The remaining participants had reintegrated mainstream schools. Among them, the proportion with grade retention and/or requiring adaptations increased from 23% to 54% between 1 and 7 years post-injury.

Outcome measures at 1 and 7 years post-injury (Table 3)

All children had some degree of functional impairment on the PIFOS (positive total score) at 1 year post-injury, with 9% presenting severe impairment and 53% mild difficulties. The mean group scores for overall disability (GOS) corresponded to moderate disability level at both times (close to GOS-Peds level 2: moderate disability at 1 year, and GOS-E moderate disability, upper level at 7 years). At 7 years post-injury, GOS-E scores were in the good-recovery range for 21 participants (upper level, $n=4$; lower level, $n=17$), moderate-disability range for 10 (upper level, $n=6$; lower level, $n=4$), and severe-disability range for 8 (upper level, $n=5$; lower level, $n=3$) (Fig. 1B). Overall disability

significantly decreased between 1 and 7 years ($F_{(1,38)}=18.14, p=0.0001$). Although 54% of participants had achieved good recovery at 7 years (vs only 13% at 1 year), disability level remained stable (49%) or worsened (5%) for more than half of the participants. Among the 34 children with moderate or severe disability at 1 year, 16 (47%) showed good recovery at 7 years.

Intellectual ability (*FSIQ*) level remained stable ($F_{(1,34)}=2.4, p=0.13$) between 1 and 7 years after TBI (Fig. 1C), with average scores about 1 SD below expected values (88 and 86.2, respectively). Overall, 14% and 11% of participants showed intellectual deficiency ($FSIQ < 70$) at 1 and 7 years, respectively. We found no significant difference between the 1- and 7-year mean parent-ratings of the executive functioning (BRIEF) and behaviour problems (C/ABCL) ($F_{(1,19)}=3.28, p=0.09$ and $F_{(1,26)}=0.22, p=0.64$) (Fig. 1D, E). The proportion of children with reported impaired executive functioning evolved from 32% to 44% and those with behaviour problems from 42% to 36%.

Factors associated with overall long-term outcome at 7 years after TBI (Appendix Table A)

Initial factors associated with long-term outcome

Overall disability (GOS-E score) was significantly associated with the severity of the polytrauma (ISS) ($r = 0.40, p=0.01$). Of note, 5 of 9 patients who underwent acute neurosurgery were in the severe disability group at 7 years (vs 3 of 30 who did not; Fisher's exact test $p=0.009$). Intellectual ability at 7 years after TBI was associated with pre-injury educational status (adaptations or grade retention) ($t = 2.42, p=0.02$). Long-term pejorative academic status was associated with the ISS ($r = 0.49, p=0.004$) and the presence of a penetrating skull fracture ($X^2=5.08, p=0.02$). The remaining socio-demographic characteristics, injury severity indices and ICU medical features were not significantly associated with long-term outcomes.

Concurrent clinical and neuropsychological factors associated with long-term outcomes

Among clinical outcomes, only the presence of post-traumatic epilepsy at 7 years was correlated with higher long-term overall disability (GOS-E score) ($t = -4.12, p=0.0002$) and with altered educational status (more need for special education, academic adaptations or grade retentions) ($X^2=8.42, p=0.004$) at 7 years after TBI. Among the 4 participants with epilepsy, 3 had severe disability and 1 moderate

disability. Greater level of long-term overall disability (GOS-E score) was strongly associated with impaired educational status ($r = 0.67, p < 0.0001$) and lower intellectual ability ($r = -0.59, p = 0.0001$) and weakly with higher (worse) executive dysfunction (BRIEF-GEC) ($r = 0.43, p = 0.01$) and behaviour problems (C/ABCL total score) ($r = 0.41, p = 0.02$). Long-term intellectual ability was strongly correlated with concurrent academic status ($r = -0.63, p = 0.0001$). The presence of behaviour problems was also associated with lower FSIQ ($r = -0.37, p = 0.04$) and altered academic status ($r = 0.39, p = 0.04$). The total BRIEF and the C/ABCL scores were highly correlated ($r = 0.86, p < 0.0001$).

Predictive value of functional status at 1 year after TBI on overall long-term outcomes (Table 4)

Table 4 presents the correlations between 1-year post-injury assessments and 7-year clinician-rated, performance and questionnaire-based outcomes. Overall disability (GOS-Peds) at 7 years after TBI was correlated moderately with the GOS and strongly with the PIFOS score and the FSIQ at 1 year post-injury. Intellectual ability (FSIQ) at 7 years after TBI was weakly correlated with the GOS score and strongly with the PIFOS score and the FSIQ at 1 year post-injury. Executive functioning at 7 years post-injury was correlated moderately with the PIFOS score and the FSIQ at 1 year post-injury, and presence of behaviour problems at 7 years post-injury was correlated moderately with the PIFOS score, FSIQ and GOS score at 1 year post-TBI.

We performed multivariate regression analyses with GOS score, PIFOS score and FSIQ collected at 1 year post-injury as explanatory variables and 7-year post-injury GOS-E score, FSIQ, BRIEF-GEC score and C/ABCL total score as dependent variables.

For overall disability at 7 years post-injury (GOS-E), the model explained 55% of the variance. Only PIFOS score assessed at 1 year-post-injury remained significantly associated with overall disability at 7 years post-TBI ($F_{(3,31)} = 13.18, p < 0.0011$). More specifically, for the 32 participants with functional assessment at 1 year, total mean PIFOS scores corresponding to the 7-year GOS-Peds* score good-recovery and moderate-disability categories were close ($n=18: 0.78$ and $n=9: 1.06$), whereas the 1-year PIFOS score corresponding to severe disability at 7 years was higher ($n=5: 2.02$). All 3 participants with total PIFOS score > 2 (severe functional impairment at 1 year post-TBI) presented severe

disability at 7 year, and all participants with scores <1.23 had good recovery or mild/moderate disability at 7 years (cut-off =1.23, sensitivity =100%, specificity =78%; positive predictive value =45%; negative predictive value =100%) (Fig. 2).

For intellectual ability at 7 years post-injury, the model explained 87% of the variance. Only FSIQ at 1 year post-injury ($F_{(3,30)}=90.96$, $p<0.0001$) remained significantly associated with FSIQ at 7 years post-injury.

For executive functions (BRIEF) and behaviour problems (C/ABCL), the models explained 27% and 34% of the variance respectively, but none of the 3 explanatory variables remained significant.

Discussion

This study reports the clinical and functional outcomes after severe childhood TBI in a relatively large group of children followed up prospectively at 1 and 7 years post-injury. The study sample was representative of the whole cohort. The results confirmed the significant medium- and long-term impact of severe TBI on a wide variety of domains of functioning and highlighted the importance of accurate longitudinal multimodal functional status assessment.

Most of the clinical impairments remained stable or evolved slightly after 1-year post-injury, whereas overall disability level (GOS) improved significantly from 1 to 7 years post-TBI, although disability levels were highly heterogeneous, ranging from satisfactory recovery for almost half of the participants, to severe persistent impairments for one fifth. Regardless of their GOS level, almost half of the participants had substantial cognitive, behaviour and/or academic difficulties at 7 years. The functional impairment severity (higher PIFOS score) and level of intellectual ability (lower FSIQ) measured 1 year post-injury seem the best predictors of the long-term overall outcome and cognitive disability level, respectively.

Clinical and functional outcomes

Our findings build on the existing literature [14,18,19,33] by demonstrating that a significant proportion of children with severe TBI present substantial functional impairments, which poorly improve after the first year. In accordance with previous studies [2,4,6,14], the present investigation

confirms the high risk of persisting (moderate or severe) disability after severe childhood TBI (1 year: 87%; 7 years: 46%), with long-lasting severe disability in almost one fifth of participants. Our results indicate the high heterogeneity of FSIQ, with no significant improvement between 1 and 7 years post-TBI, and average scores remaining 1 SD below expected values, as already reported [7,9,14,34]. Furthermore, significant deficits in executive functioning were evident at both times, as previously reported [35-37], which suggests a possible lack of expected gains with age and/or increased deficits over time, when environmental demands increase [38]. Our results also indicate poor behaviour outcome for almost 2 in 5 participants, which is consistent with other studies reporting long-lasting behaviour problems after childhood severe TBI [2,6,9,34,39,40], with obvious negative consequences on daily life and expected social outcome and participation in adulthood [5,41].

Our results confirm previous reports of poor academic outcome after severe TBI [10,11] in that more than half of the children who reintegrated mainstream schooling repeated a grade and/or needed educational interventions, and almost one quarter enrolled in an educational program required special education services at 7 years post-TBI. The proportion of participants requiring special education tended to decrease from 1 to 7 years, which was mainly due to the discharge of patients still hospitalized in the rehabilitation ward at 1 year post-injury (where they also received special education). After discharge, patients who were oriented toward special education usually remained in this status over time.

Overall, our findings confirm persistent functional difficulties after severe childhood TBI, especially in neuropsychological, behaviour, adaptive and academic domains [2,4,5,41,42], with possible delayed onset [2,6]. These difficulties may persist several decades post-injury [5,41,42], which highlights the need for long-term follow-up.

Factors associated with overall long-term outcome at 7 years post-injury

Early prognostic factors of long-term outcomes

Contrary to what was expected from previous studies [33,43-45], few of the early variables (socio-demographic factors, pre-traumatic functioning, age at injury, as well as TBI characteristics and initial

medical ICU data) were significantly associated with long-term outcomes in this exclusively severe TBI sample. Only some markers of initial injury severity (ISS, penetrating skull fracture and the need for early neurosurgical intervention) were significantly associated with the level of disability or with poor academic outcome at 7-years. Other than the lack of statistical power related to sample size, we suggest that initial severity plays a major role in the acute and subacute phases of recovery, whereas long-term functional evolution, being much more complex and multifactorial, is highly affected by other environmental and evolutionary criteria, which can moderate the influence of early factors. These results corroborate other studies (involving adult cohorts) showing that correlations between initial and late variables can be very low [46], with only 35% of long-term observations predicted by initial (clinical and radiological) severity indices [47].

Concurrent factors associated with long-term outcome

Overall disability at 7 years post-injury was significantly correlated with altered intellectual ability, poor academic status, executive dysfunction and behaviour issues. These associations are probably due to the assessment properties of the GOS-E scale, which take into account autonomy in basic and instrumental activities of daily living, academic difficulties/type of schooling and leisure activities, which are frequently disrupted by cognitive and behaviour disorders. Conversely, overall disability at 7 years post-injury was not associated with clinically rated impairments, other than post-traumatic epilepsy.

Long-term intellectual ability was correlated strongly with the type of ongoing education and weakly with behaviour problems. We also observed significant associations between academic outcome and post-traumatic epilepsy as well as with behaviour problems. These results allow for confirming that academic outcome is strongly affected by cognitive functioning [48] and highlight the deleterious effects of severe TBI on long-term learning abilities and academic performance [10,11,49].

Predictive value of functional status at 1 year post-injury on 7-year disability level

Long-term overall disability (GOS-E) was strongly predicted by level of functional impairment at 1 year post-injury (with a clear cut-off on the PIFOS score discriminating participants with severe disability at 7 years post-TBI). Before the multivariate regression analysis, the disability level at 7 years post-injury

was also strongly correlated with poorer 1-year intellectual ability and weakly with 1-year GOS-Peds score. These results might be explained by the accuracy of the functional assessment provided by the PIFOS, which appears to be a reliable multidimensional scale that could better capture the full spectrum of overall “disability” as defined by the World Health Organization [50] and injury-specific sequelae after pediatric brain injury [17,18]. Indeed, the PIFOS accounts for a more “subjective” approach to the parents’ point of view, probably depicting a more accurate portrait of the patient's everyday level of functioning, unlike the objective (but sometimes incomplete) assessment that can be obtained from specific medical assessments and the GOS score.

Limitations

The interpretation of the current results should take into account certain limitations that might restrict the generalizability of the present findings. First, as commonly seen in longitudinal cohorts, 40% of participants were lost to follow-up between 1 and 7 years. However, the study sample was representative of the initial cohort. Also, even if the analysis sample was relatively large as compared with other studies and was drawn from a significant prospective longitudinal cohort of patients who sustained severe pediatric TBI, the overall sample size remained small. Thus, we performed some comparisons of relatively small groups, which reduced the power of the analyses (e.g., pre-injury or injury characteristics). Despite the small number of participants with long-term severe disability, we observed significant associations with functional outcome and intellectual ability measured at 1 year post-TBI, which confirms the strength of this predictive relationship.

Finally, our results regarding academic status warrant some caution in interpretation. Academic status does not take into account the reasons for orientation toward special education (e.g., motor and/or cognitive deficits) and is not an accurate reflection of actual academic abilities. Furthermore, those results rely on cultural and organizational issues of the French educational and medico-social systems, which cannot necessarily translate to different systems.

Conclusions

This study adds to the literature on examining the significant impact of childhood severe TBI on medium- and long-term overall and functional outcomes. It illustrates the public health impact, particularly related to the long-lasting sequelae, including negative socio-behaviour and cognitive outcomes, highly associated with disabling difficulties in academic/vocational performance, participation, and peer relationships. However, our results also indicate high variability of the outcomes, with a significant proportion of children with severe TBI demonstrating surprisingly few functional deficits and good overall long-term outcomes. Our results also highlight the need for clinicians to provide careful evaluation and adequate follow-up for patients with severe TBI, especially those presenting persistent significant functional deficits at 1 year post-injury who should benefit from careful monitoring and follow-up.

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Conflict of interest. None declared.

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in Belfast in September 2018, the 31st European Academy of Childhood Disability meeting in Paris in May 2019, and the *Journées Parisiennes de Pédiatrie* (French pediatric conference) in Paris in December 2021, and will be presented at the *Société Française de Neurologie Pédiatrique* (French Society of Pediatric Neurology) congress in Angers in February 2022.

Figure legends

Figure 1. Evolution from 1 to 7 years after traumatic brain injury (TBI) of the main (clinically rated, performance- and questionnaire-based) outcomes for participants (n=39). A) Academic status at 1 and 7 years post-injury. Mainstream school, with or without the need of any type of adaptation (A) and/or grade retention (R), versus special education. B) GOS-Peds*: overall disability level. To compare the GOS (Glasgow Outcome Scale) scores between 1 and 7 years post-injury, we converted the 7-year GOS-E (GOS-Extended) scores (8 levels) into the 5 categories of the GOS-Peds assessed at 1 year post-injury (GOS-Peds*). C) Full-Scale Intellectual Quotient (FSIQ) variability. Mean expected score in general population =100 (solid line); <85 (-1 SD: lower densely dashed line); <70 (-2 SD: lower loosely dashed line). D) Behavior Rating Inventory of Executive Functions (BRIEF): parent-rated executive functioning in everyday life. Mean expected score in general population: T-score =50. Clinical cut-off score ≥ 65 (+1 SD: dashed line). E) Child/Adult Behavior Checklist (C/ABCL): parent-rated everyday behavior. Mean expected score in general population: T-score =50. Clinical cut-off score ≥ 65 (+1 SD: dashed line).

Figure 2. Mean total scores on the Pediatric Injury Functional Outcome Scale (PIFOS) at 1 year post-injury according to the degree of overall disability at 7 years post-TBI for participants (n=32). All 5 participants presenting severe disability level at 7 years post-injury had a total PIFOS score at 1 year ≥ 1.23 (1.23, 1.46, 2.08, 2.5, 2.81). Of the participants with long-term good recovery or moderate disability, 20 (74%) had a PIFOS score <1.23, and the other 7 (4 with moderate disability, and 3 with

good recovery) had a PIFOS score 1.23 to 1.73. Cut-off = 1.23, sensitivity = 5/5 (100%), specificity = 21/27 (78%); positive predictive value = 5/11 (45%); negative predictive value = 21/21 (100%).

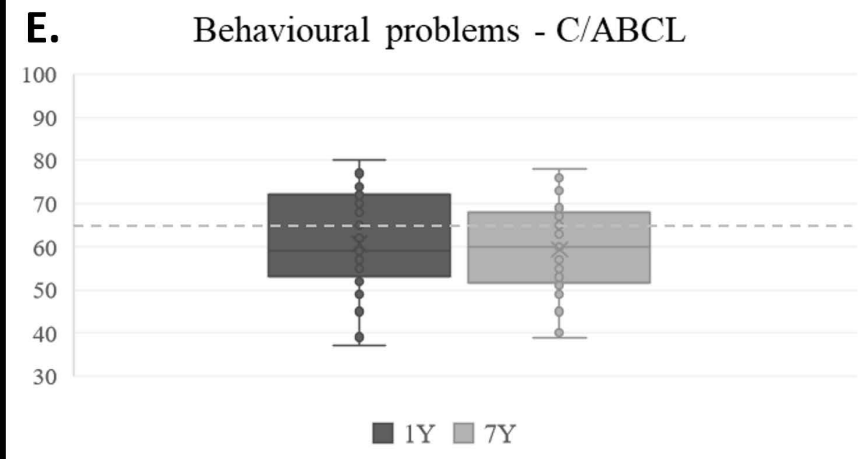
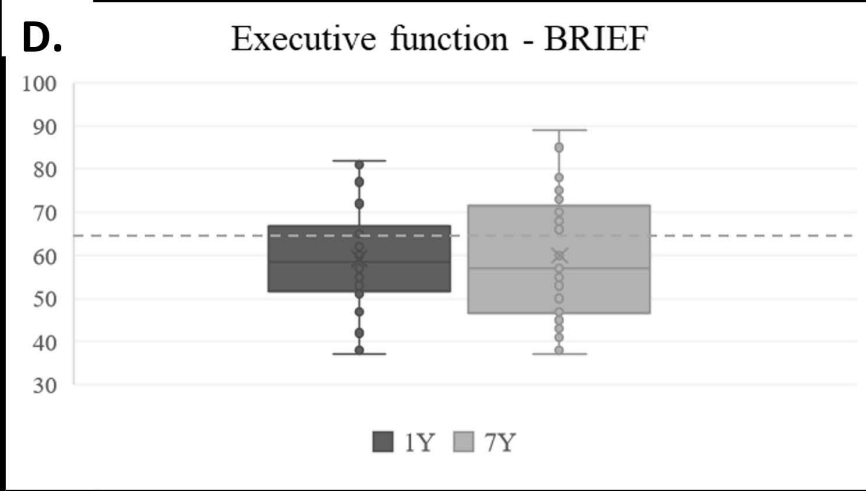
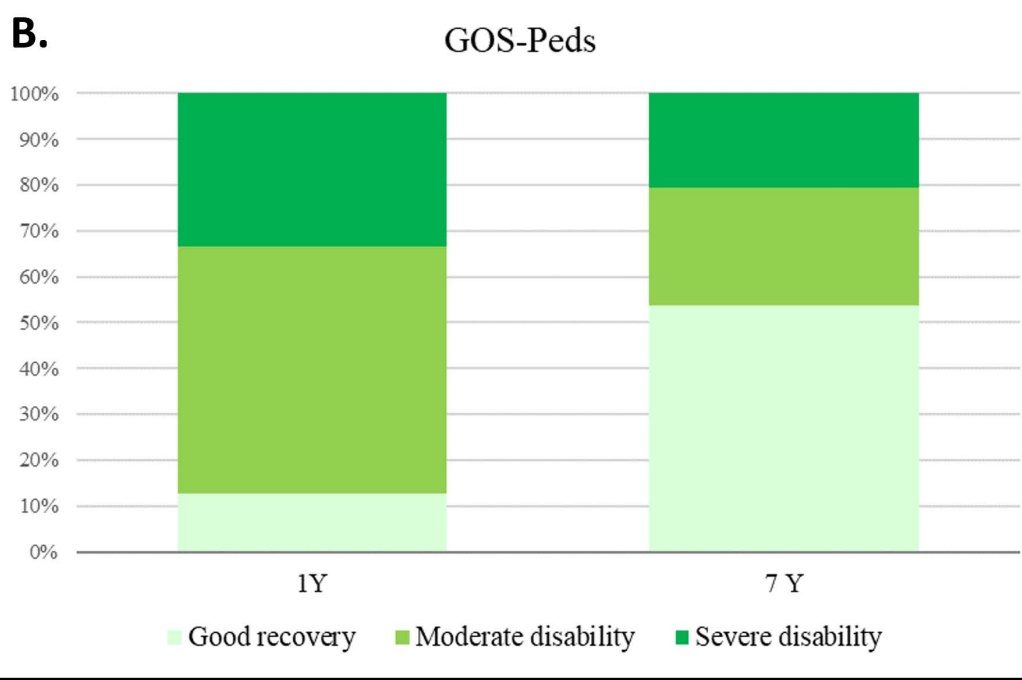
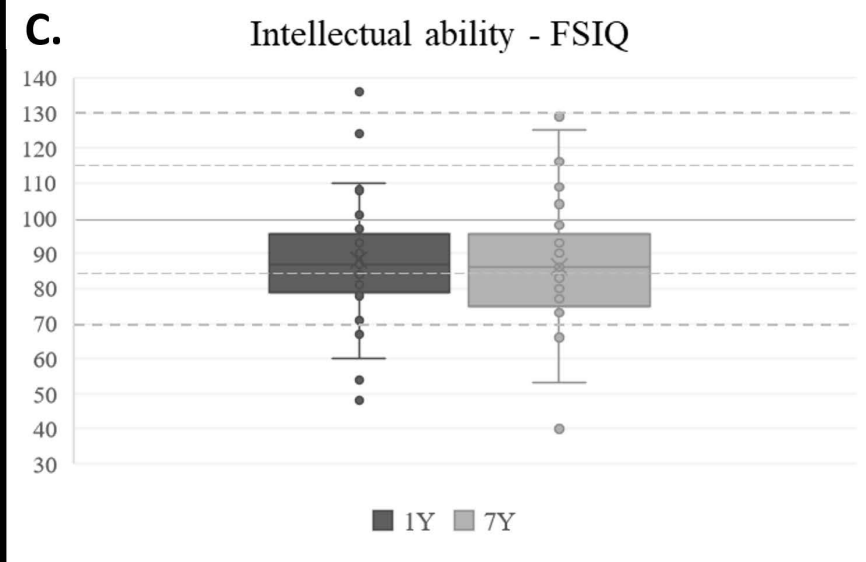
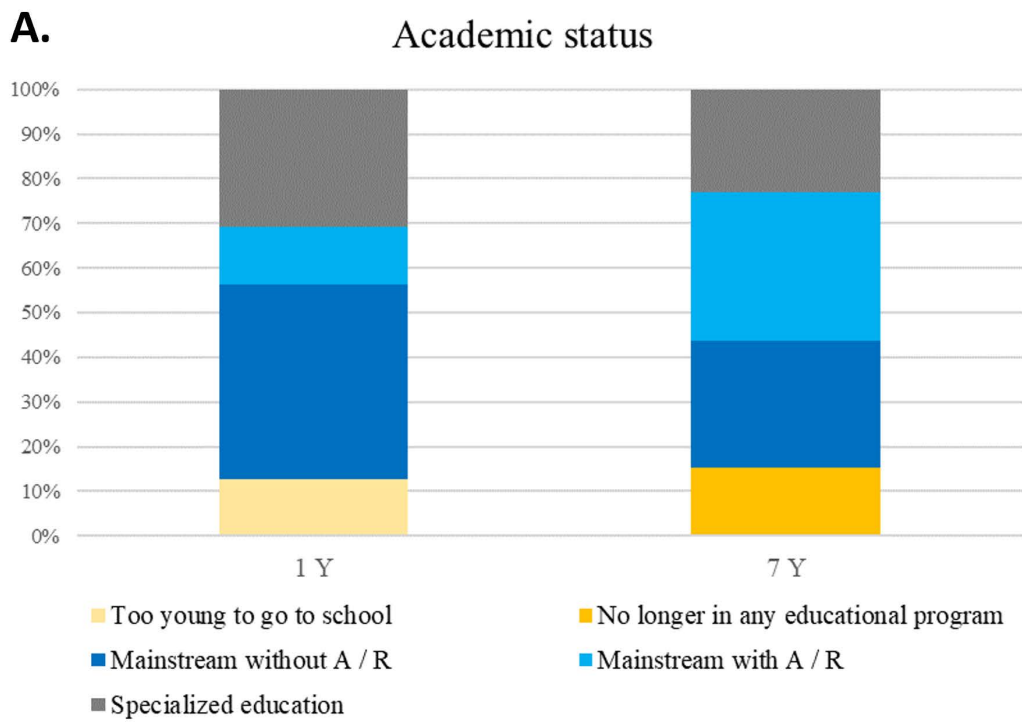
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□ Good recovery / Moderate disability - 7Y

■ Severe disability - 7Y

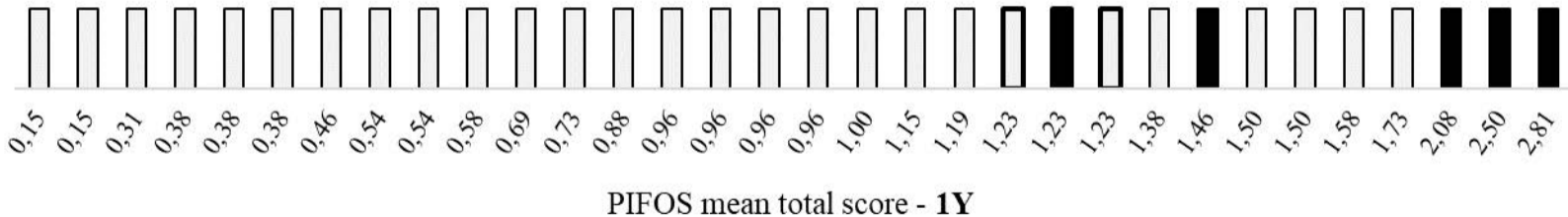


Table 1. Sociodemographic, initial injury severity and injury-related outcomes of the study participants with severe traumatic brain injury (TBI) ($n=39$).

Follow-up 7 years after TBI	n (%)	Mean (SD)	Range
Sociodemographic characteristics			
Age at injury (years)		7.6 (4.6)	0.3–14.7
Age at long-term assessment (years)		15.4 (4.4)	7.4–22.7
Time since injury		7.8 (0.8)	5.9–9.3
Adults (≥ 18 years old)	14 (36)		
Sex, male	25 (64)		
Parental education level (medium-high ^a)	20 (51)		
Marital status (parents living together)	26 (67)		
Number of siblings		3.7 (1.4)	1–6
Language spoken at home (only French)	20 (51)		
Preinjury education (grade retention/adaptation)	5 (13)		
Preinjury medical history	8 (21)		
Initial injury severity			
Lowest Glasgow Coma Scale Score		5.8 (1.7)	3–8
Pediatric Trauma Score		3.9 (2.3)	-1–9
Injury Severity Score		27.9 (9.9)	4–50
Length of coma (days)		6.7 (4.9)	1–22
Injury-related characteristics			
Intracranial hypertension (yes) *	17 (46)		
Brain hypoperfusion (yes) *	31 (84)		
Collapsus (yes)	6 (15)		
Penetrating skull fracture (yes)	9 (23)		
Neurosurgery in acute phase	9 (23)		

^a At least one of the parents had graduated from high school.

* One or two missing values.

Table 2. Clinical impairments, medical management and academic status at 1 and 7 years after severe TBI ($n=39$).

	1 year		7 years	
	N	(%)	N	(%)
Clinical impairments				
<i>Post-traumatic epilepsy</i>	3	(8)	4	(10)
<i>Locomotor disability</i>				
Motor deficits	14	(36)	10	(26)
Paraplegia (spinal cord injury)	1	(3)	1	(3)
Hemiplegia or significant hemiparesia / Cerebellar signs	8 / 10	(21) / (26)	6 / 6	(15) / (15)
Walking [⊖] , with / without technical device	3 / 35	(8) / (92)	2 / 36	(5) / (95)
<i>Sensory / Visual / Hearing deficits</i>	2 / 7 / 4	(5) / (18) / (10)	1 / 7 / 4	(3) / (18) / (10)
<i>Urinary incontinence</i>	5	(13)	1	(3)
Surgical management				
At least 1 surgery linked to TBI sequelae	2	(5)	7	(18)
Neurosurgery / Ophthalmology	1 / -	(3)	2 / 4	(5) / (10)
Academic status				
Ongoing education	34	(87)	33	(85)
<i>Mainstream education</i>	22	(56)	24	(62)
Without A - R	17		11	
With A and/or R	5		13	
With adaptations	4		5	
With grade retention	-		2	
With adaptations and grade retention	1		6	
<i>Special education</i>	12	(31)	9	(23)
Within the rehabilitation department	11		-	
Special education center/class	1		9	
<i>Too young to go to school</i>	5	(13)	-	
No longer in any educational program	-		6	(15)
High-school vocational diploma / lower vocational training diploma	-		2 / 3	
School failure and dropout	-		1	

(%): the percentages correspond to the proportion in relation to the 39 participants, unless there are missing data, and for the variable that excludes the paraplegic patient (⊖). Percentages by sub-total sections are not presented.

A - R: adaptation and/or grade retention

Table 3. Outcome measures at 1 and 7 years after severe TBI ($n=39$).

<i>Outcome scales</i>	1 year			7 years		
	n (%)	Mean (SD)	Range	n (%)	Mean (SD)	Range
PIFOS total score	32	1.1 (0.6)	0.2–2.8		-	
Severe impairment [2–4]	3 (9)					
Moderate impairment [1–2]	12 (38)					
Mild difficulties [0–1]	17 (53)					
GOS-Peds/GOS-E Peds*	39	2.2 (0.7)	1–3	39	1.7 (0.8)	1–3
1. Good recovery	5 (13)			21 (54)		
2. Moderate disability	21 (54)			10 (26)		
3. Severe disability	13 (33)			8 (20)		
Intellectual ability: FSIQ	37	88.0 (18.6)	48–136	37	86.2 (17.8)	40–129
> +1 SD (> 115)	3 (8)			3 (8)		
Average (85–115)	18 (49)			16 (43)		
< -1 SD (< 85)	16 (43)			18 (49)		
< -2 SD (<70)	5 (14)			4 (11)		
Executive Function: BRIEF	22	59.2 (12.7)	37–82	34	59.9 (14.3)	37–89
GEC ≥ 65 (impaired)	7 (32)			15 (44)		
Behavior: C/ABCL	31	60.7 (11.2)	37–80	33	59.3 (10.4)	39–78
Total score ≥ 65 (impaired)	13 (42)			12 (36)		

BRIEF, Behavior Rating Inventory of Executive Function; Parent-reports (GEC, Global Executive Composite); C/ABCL, Child/Adult Behavior Checklist, Parent-reports (total score); FSIQ, Full Scale Intellectual Quotient (Wechsler scales); GOS-Peds, Pediatric Glasgow Outcome Scale (5 levels); GOS-E (Peds), (Pediatric) Glasgow Outcome Scale - Extended (8 levels); GOS-Peds*, GOS-E results collapsed into GOS-Peds categories (5 levels); PIFOS, Pediatric Injury Functional Outcome Scale (total score)

Table 4. Correlations of clinician-rated, performance and parental questionnaire-based outcomes assessed at 7 years after TBI with functional status at 1 year.

7-year post-TBI outcomes												
	<i>Clinician-rated</i>			<i>Performance-based</i>			<i>Questionnaire-based</i>					
	Overall disability			Intellectual ability			Executive functions			Behavior		
	(GOS-E)			(FSIQ)			(BRIEF -Parents) GEC			(C/ABCL -Parents) Total problems		
1-year assessments	N	r	P value	N	r	P value	N	r	P value	N	r	P value
Functional outcome												
PIFOS <i>total</i>	32	0.62	0.0002	31	-0.56	0.001	28	0.53	0.004	27	0.57	0.002
Overall disability												
GOS-Peds	39	0.47	0.002	37	-0.34	0.04	34	0.32	<i>ns</i> (0.06)	33	0.41	0.02
Intellectual ability												
FSIQ	37	-0.64	<0.0001	35	0.87	<0.0001	32	-0.44	0.01	31	-0.52	0.003

BRIEF, Behavior Rating Inventory of Executive Function; Parent-reports (GEC, Global Executive Composite); C/ABCL, Child/Adult Behavior Checklist, Parent-reports (total score); FSIQ, Full Scale Intellectual Quotient (Wechsler scales); GOS-E, Glasgow Outcome Scale-Extended, Adult/Pediatric versions; GOS-Peds, Pediatric Glasgow Outcome Scale; *ns*, non-significant; PIFOS, Pediatric Injury Functional Outcome Scale (total score); *r*, Pearson correlation coefficient