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Functional outcome after severe childhood traumatic brain injury: results of the TGE prospective longitudinal study

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ABSTRACT

Background. Childhood severe traumatic brain injury (TBI) is a leading cause of long-lasting acquired disability, but little is known about functional outcome.

Objective. We aimed to 1) study clinical recovery and functional outcome over 24 months after severe childhood TBI, 2) identify early sociodemographic and severity factors influencing outcome, and 3) examine the clinical utility of the Pediatric Injury Functional Outcome Scale (PIFOS) to assess functional outcome.

Methods. Children (0-15 years) consecutively admitted in a trauma centre after accidental severe TBI over 3 years were included in a prospective longitudinal study (Traumatisme Grave de l'Enfant cohort). We measured clinical/neurological recovery, functional status (Pediatric Injury Functional Outcome Scale, [PIFOS]), overall disability (pediatric Glasgow Outcome Scale [GOS-Peds]) as well as intellectual ability (Wechsler scales) and educational outcome (mainstream school vs special education) of survivors at 1, 3, 12 and 24 months post-injury.

Results. For 45 children (aged 3 to 15 years at injury), functional impairments were severe within the first 3 months. Despite the initial rapid clinical recovery and significant improvement over the first year, substantial alterations persisted for most children at 12 months post-TBI, with no significant improvement up to 2 years. Up to 80% of children still had moderate or severe overall disability (GOS-Peds) at 24 months. The severity of functional impairments (PIFOS) at 12 and 24 months was mostly related to socio-emotional, cognitive and physical impairments, and was significantly correlated with clinical/neurological deficits and cognitive (intellectual, executive) and behavioural disorders. Initial TBI severity was the main prognostic factor associated with functional status over the first 2 years post-injury.

Conclusions. Our results confirm the significant impact of severe childhood TBI on short- and medium-term functional outcomes and overall disability. All patients should benefit from

systematic follow-up. The PIFOS appeared to be an accurate and reliable tool to assess functional impairment evolution and clinically meaningful outcomes over the first 2 years post-injury.

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

Introduction

Childhood traumatic brain injury (TBI) remains a worldwide leading cause of mortality and acquired long-term disability [1,2]. Children with severe TBI, defined by Glasgow Coma Scale (GCS) score ≤ 8 [3], have the worst expected long-term outcomes as compared with those with less severe TBI [4], although it remains difficult to predict outcome at the early phase.

Because the injury occurs in a developing brain, the acquired lesions can disrupt subsequent brain development, with delayed consequences emerging over time, causing significant short- and long-term alterations in a wide range of functional abilities [1,5,6]. The significance of disabling impairments might not be realized until years after the injury, when higher-level cognitive and behavioural functioning is required to meet typical developmental milestones [5,7]. This situation can result in changes that affect the child's daily activities, cognitive, behavioural and school functioning [8–10], with consequences extending to later social integration and overall participation [1,11,12].

Children with severe TBI have substantial neuropsychological impairments initially, with significant improvement during the first year post injury, followed by negligible subsequent improvement [13–15]. Overall, most children experience persistent disability at 1 year after severe TBI, especially in the cognitive, behavioural, emotional and social domains [6,15–18].

Outcomes after TBI are heterogeneous and can be assessed with various criteria, including clinical and neuropsychological assessments, social/academic status, and self- and proxy-completed questionnaires assessing various domains of functioning. The Glasgow Outcome Scale (GOS) allows for an overall outcome assessment after TBI [19] based on objective criteria. Although it is simple and useful for global outcome studies, its broad categories insufficiently account for the multidimensional nature of TBI outcomes and have limited sensitivity to change within specific functional domains [20].

The Pediatric Injury Functional Outcome Scale (PIFOS) [21] was developed in response to the need for a comprehensive, reliable and easy-to-apply multidimensional functional outcome scale capturing the full spectrum of “disability” (as defined by the WHO, 2001). The PIFOS allows for measuring the amount and the evolution of the overall burden and injury-specific sequelae in various domains of functioning, across developmental states after pediatric brain injury. The PIFOS items assess change (relative to pre-injury performance) in various domains relevant to children’s everyday functioning (see below) based on objective as well as more subjective criteria (parental evaluation). The PIFOS is appropriate for use in a large age range, after any TBI severity, and has good psychometric properties, including sensitivity to change. As such, it may be a useful injury-specific tool to assess the impact of injury in children at different developmental levels [21]. However, few studies have used the PIFOS to assess detailed specific and overall functional outcomes and their evolution over time after severe pediatric TBI. For instance, the PIFOS was previously used as a measure of pre-injury functioning [22,23], pre-injury fatigue [24] or as an additional tool used to validate an acute composite injury severity score [25]. Only more recently have several reports indicated that the PIFOS total score was associated with distinct outcomes 2 and 7 years after severe pediatric TBI, namely quality of life, participation, memory and executive functions [12,26–28]. Hence, the present study sought to add evidence regarding the PIFOS

appropriateness in assessing functional outcomes after severe pediatric TBI as well as examine its correlates and evolution over time during the initial 2 years post-injury.

The aims of this prospective cohort study were to 1) study clinical/neurological impairments and functional outcome, and evolution of the different clinical deficits and functional domains over 24 months after severe childhood TBI; 2) identify sociodemographic and injury severity-related factors associated with those outcomes; and 3) examine the clinical utility of the PIFOS in assessing functional status over 24 months post severe TBI.

Methods

Participants

Children 0 to 15 years old who were consecutively admitted over a 3-year period to the pediatric neurosurgical intensive care unit at Necker Enfants Malades Hospital within the first 6 hr after severe accidental TBI (GCS score ≤ 8 and/or Injury Severity Score [ISS] >16). Children with no vital signs on admission or inflicted head injury were not included. All 81 children initially enrolled received treatment according to international guidelines for the management of severe TBI [29]. A total of 65 (80%) survived the acute period and 62 (95.4%) were assessed up to 24 months. To analyse the functional outcome using the PIFOS, we focused on the 52 patients who were within the validated scale age range (3 to 15 years at injury), among whom we retained for analyses the 45 patients with no missing data at any time point (86.5% of eligible children; Fig. 1).

Measures

Sociodemographic characteristics and pre-injury history: gender, age at injury, parental education level (medium-high: at least one parent had graduated from high school; low: none of the parents had a high school diploma) and pre-injury academic status (child had

difficulties requiring extra help at school, assisted, and/or had stayed back 2 year, delayed, according to parental reports vs normal).

Injury severity was assessed by the lowest GCS score measured within the first 24 hr after TBI [3], initial ISS [30], initial Pediatric Trauma Score (PTS) [31], and length of coma (corresponding to the day of spontaneous eye opening).

Injury-related features: medical data were collected during the acute intensive care unit phase, including the presence of penetrating skull fracture, intracranial hypertension, collapsus/hypotension, brain hypo-perfusion, seizures (see [27] for more details; see Table 1).

Follow-up measures and procedures: prospective follow-up was performed at 1, 3 months (short-term), 12 and 24 months (medium-term outcomes) in the pediatric rehabilitation department of the Saint Maurice Hospitals. At each time point, the child underwent a detailed medical interview (e.g., ongoing treatments, including anticonvulsant treatment for post-traumatic epilepsy) and neurological examination (e.g., consciousness level, ability to follow simple commands, presence of motor deficit [hemiplegia, hemiparesis], signs of cerebellar dysfunction, sensory deficits), ability to maintain head and sitting position, walk (with or without help), sphincter control and type of feeding (normal or use of thickened food/liquids or feeding tube). Children were assessed on a different day by a trained child neuropsychologist who performed a comprehensive neuropsychological assessment (at 3, 12 and 24 months), using a combination of standardized neuropsychological tests (e.g., measurement of the child's intellectual ability, memory, attention, and executive functions), standardized questionnaires answered by the parents and standardized scales (see below) completed during a semi-structured interview with parents.

Types and amount of ongoing rehabilitation therapies and educational status (e.g., returned to mainstream school with or without the need for any type of adaptation and/or grade retention; versus special education within a specialized school or within the rehabilitation department), were collected at 12 and 24 months (see Table 2).

This study was approved by the Comité de Protection de Personnes d'Île-de-France VI (CPP IDF VI) ethics committee, and parents gave their informed written consent.

Outcome measures

Overall level of disability was assessed with the Glasgow Outcome Scale (GOS [19]) adapted for the pediatric population [32] (GOS-Peds), yielding 4 categories, other than death (1, good recovery; 2, moderate disability; 3, severe disability; 4, vegetative state).

Functional outcome was assessed with the PIFOS [21], a brief injury-specific multidimensional rating scale for children aged 3 to 15 years, completed by a trained health care provider during a structured interview with parents. This scale assesses performance in relation to pre-injury levels of functioning. We used the PIFOS version that was available at the time of the study start. The scale consists of 26 items, rating 6 areas of function (motor, daily living, communication skills, social-emotional, cognition/academic functioning, and physical changes) on a four-point Likert scale (0, no change from pre-injury levels; 2 to 4, increasing need for support and significant functional limitations), higher PIFOS scores reflecting greater difficulties (range of total raw scores [0-104]). Mean item scores are presented for the 6 sub-scale scores and total score (0-1, absence or mild difficulties; 1-2, moderate impairment; 2-4, severe to very severe impairment).

Intellectual ability: Full Scale Intellectual Quotient (FSIQ) (mean=100; SD=15) was measured by using age-appropriate French versions of the Wechsler Scales, namely, Wechsler Intelligence Scale for Children – III (WISC III [33]) and Wechsler Preschool and Primary Scale of Intelligence - III (WPPSI-III [34]).

Executive functioning was measured with the French adaptation of the parent-reported form of the Behavior Rating Inventory of Executive Functions (BRIEF) in participants aged 5 to 18 years [35]. The total score [Global Executive Composite index (GEC)], expressed as a *T*-score (mean=50, SD=10) was used as the outcome, higher scores indicating worse executive functioning, and a *T*-score ≥ 65 considered clinically significant.

Behavioural problems were assessed with age-appropriate versions of the parent-reported form of the Achenbach Child Behavior Checklist (CBCL) [36]). Total, internalizing and externalizing problems *T*-scores are reported here (mean=50, SD=10); higher scores reflect more pronounced behaviour problems and a *T*-score ≥ 65 is considered clinically significant.

Data analysis

Data analysis was performed with SAS v9. Descriptive statistics were used to describe sociodemographic and medical characteristics and the main outcomes (including PIFOS scores) at each time point. Continuous variables are expressed with mean, standard deviation (SD) and range; categorical variables are expressed with number and percentage. Univariate statistical analyses (Student *t*-test, paired *t*-test, Pearson correlation, chi-square or Fisher exact test, repeated measures ANOVA and regression analyses) focused on the evolution of the main outcomes across the time periods and associations with the PIFOS score. Internal consistency of the PIFOS was examined with the Cronbach alpha. A mixed model, with random effects for intercept and slope, was used to analyse the evolution of the 6 PIFOS sub-scores from 1 to 24 months. Statistical significance was 2-tailed and set at $p < 0.05$.

Results

Sociodemographic, pre-injury characteristics and initial injury severity

Table 1 summarises the sociodemographic and initial injury-related characteristics of the 45 participants. All children were aged 3 to 15 years at the time of injury and had an initial GCS ≤ 8 except one (GCS=9, with ISS score > 16). The 7 patients who were not included in the analyses did not differ significantly from those included in any of the pre-injury, demographic, or injury-related features.

Evolution of clinical assessment, disability and functional outcomes over the first 2 years

Table 2 summarises the evolution of clinical/neurological impairments, medical/rehabilitation needs and educational status from 1 to 24 months post-injury. Overall clinical impairments and care needs improved over time. The ability to follow simple commands was quite impaired at 1 month post-injury but improved rapidly, with all children displaying normal consciousness levels at 24 months post-TBI. Post-traumatic epilepsy appeared in 3 (7%) children at 12 and 24 months post-injury and required treatment. The frequency of motor deficits (presence of motor deficit, and/or cerebellar dysfunction) decreased from 1 month (47%) to 24 months (11%) post-TBI. All children had recovered head and trunk control at 3 months. At 1 year post-TBI, all patients had achieved independent ambulation, with 7% requiring assisting devices. Neurosensory deficits were among the less frequent impairments, with 2 (4%) children having persisting somatosensory deficit and 3 (7%) presenting visual impairment (2 had oculomotor nerve palsy and 1 unilateral blindness after optic nerve damage) at 12 and 24 months post-injury. More than one quarter of the patients initially required monitoring of swallowing deficits, but all had recovered this function by 12 months. The most frequent rehabilitation therapies still in place at 1 and 2 years post-injury were speech-language therapy, occupational therapy and physiotherapy. The proportion of children needing psychological support and/or psychiatric follow-up decreased from 12 (47%) to 24 months (27%).

Among the 44 children with available educational status data at 1 year, 23% attended a mainstream school with adaptations and/or grade retention; 30% still attended school within the rehabilitation department, and 9% had been referred for special education. These proportions were 32%, 9% and 16% at 2 years, with 1 participant enrolled in a technical professional certification and 1 who had dropped out of school after socio-behavioural issues. Finally, 36% had favourable academic outcome (mainstream school without any adaptation or grade retention) at 2 years.

Figure 2 shows the evolution of post-injury outcomes (clinician-rated, performance- and questionnaire-based) from 1 or 3 months to 24 months post-TBI. Overall disability, assessed by the GOS-Peds (Fig. 2A), significantly decreased between 1 and 24 months ($F(2,82)=11.06$, $p<0.0001$). Among the 34 children who were severely disabled at 1 month (i.e., vegetative state and severe disability, 76%), all emerged from vegetative state by 3 months, but only 3 had good recovery at 12 months and 4 at 24 months. Although GOS-Peds scores for 47% of children improved between 1 and 3 months, nearly 95% of children still had moderate or severe disability at 3 months. At 12 and 24 months, 33% and 18% of children were in the severe disability category, respectively. Overall, the GOS-Peds scores improved significantly between 12 and 24 months ($F(1,44)=4.98$, $p<0.031$), due mostly to a shift from the severe to moderate disability categories. In contrast, the proportion of patients who reached “good recovery” remained stable between 12 and 24 months (18% and 20%, respectively) and represented a minority of patients.

The PIFOS scale (Fig. 2B) showed a unidimensional structure with good internal consistency, which justified the computation of a total score [Cronbach alpha = 0.94 (1-month), 0.86 (3 months), 0.89 (12 months), 0.91 (24 months)]. All children had some degree of functional impairment on the PIFOS (positive total score) at 1 and 3 months post-injury. All scores of functional disability rapidly improved between 1 and 3 months ($p<0.0001$, paired t-tests). Motor skills, communication and total scores decreased significantly between 3 and 12 months ($p=0.001$). There was no further significant progression from 3 to 12 months and from 12 to 24 months. Only 2 patients (4%) had a null score (no functional deficit at all) at 12 months and 3 (7%) at 24 months.

Greater difficulties were noted during the first months for motor skills, social-emotional, cognitive-academic and physical changes sub-scores. At 24 months, the main persistent

significant difficulties were for cognitive-academic, social-emotional, and physical (e.g., pain, fatigue) items.

Statistical analysis using a mixed model, with a random intercept and slope, showed a significant effect of sub-score type ($F(5,220)=473.3$, $p<0.0001$), period ($F(3,132)=19$, $p<0.0001$) and sub-score by period interaction ($F(15,660) = 3.1$, $p<0.0001$). All sub-scores significantly improved from 1 to 3 months post-injury (paired t-test, $p<0.0001$), but only communication and motor scores improved from 3 to 12 months ($p<0.001$). We found no significant difference between 12 and 24 months for any sub-score. Daily living skills and motor skills items presented the greatest recovery between 1 and 24 months.

Intellectual ability (FSIQ) (Fig. 2C) increased significantly from 3 months (mean 84.1, i.e., 1 SD below expected values) to 24 months (mean 90.9) post-injury ($F(2,82)=14.64$, $p<0.0001$). Nine of 42 children showed intellectual deficiency (IQ <70) at 3 months (21%), 5/44 (11%) at 12 months, and 3/43 (7%) at 24 months.

Regarding everyday executive functioning and behaviour, the 3, 12 and 24 months' mean parent-ratings of the BRIEF and CBCL did not differ, nor did the proportions of children with reported impaired executive functioning (BRIEF-GEC ≥ 65 : 13%, 18% and 16%, respectively) or behavioural problems (CBCL ≥ 65 : 20%, 33% and 22%) (Fig. 2D, E).

Factors associated with functional outcome

Table 3 describes the factors associated with functional outcome (PIFOS total score) at each time point.

Sociodemographic, injury severity and medical characteristics

Poorer functional outcomes (higher PIFOS scores) assessed at 1, 3, 12 and 24 months post-TBI were strongly associated with longer length of coma and were significantly associated with higher ISS and lower GCS. On regression analysis with GCS, ISS and length of coma as explanatory variables, only length of coma remained significant. Age at injury and PTS were

not significantly associated with the PIFOS score at any time.

Only child pre-injury education status was positively associated with functional outcome at 12 months post-injury ($p=0.04$). None of the other sociodemographic features or injury-related medical characteristics (other than severity markers) were significantly associated with functional outcomes at any time point.

Concurrent outcomes

Poorer functional outcome (higher PIFOS score) was strongly associated with increased overall disability (GOS-Peds) at all time points and with the presence of motor deficits (at 1, 3 and 12 months) and epilepsy (at 12 and 24 months) and was significantly associated with lower intellectual ability and increased impairments on executive functioning and behavioural problems at 3, 12 and 24 months post-TBI.

Discussion

This study reports the clinical and functional outcomes and associated factors over the first 2 years after severe TBI in a large pediatric cohort. We confirmed the multi-dimensional nature of TBI outcomes and the significant long-lasting impact of injury on a wide variety of outcome domains. Functional outcome measured by the PIFOS was severely impaired overall, with significant progression between 1 and 12 months but no significant further improvement between 12 and 24 months post-injury. Our results also highlighted the high variability between participants and the heterogeneous patterns of recovery of different functional areas for the same individual.

Short and medium-term outcomes

Our findings build on the existing literature [4,37,38] by demonstrating that a significant proportion of children with TBI present initial substantial deficits. They show overall improvement during the first year after severe TBI (clinical recovery particularly evident over

the first 3 months in some areas, including motor skills, walking, activities of daily living, and even the cognitive domain) but without significant functional progress (according to the PIFOS) during the second year post-injury, in accordance with previous studies [13–15,39]. Conversely, overall disability assessed by the GOS-Peds improved slightly during the second year post-injury. This finding suggests that the GOS-Peds might be more sensitive to change over time as compared with the PIFOS, at least in the medium-term. However, the improvement observed in the GOS-Peds was mainly due to a shift from the severe to moderate disability category, whereas the proportion of patients reaching “good recovery” remained stable, about only one-fifth of the group. This finding could be related in part to the rating of the GOS-Peds categories. Patients referred for inpatient rehabilitation are rated with “severe disability” and those receiving outpatient rehabilitation are rated with “moderate disability”. Because most patients were initially hospitalised in a rehabilitation department, their progress and discharge might have explained some of the improvement observed in the GOS-Peds ratings. As compared with the GOS-Peds, the PIFOS is completed during a semi-structured interview with parents and covers a number of functional domains of daily living, including cognitive and behavioural functioning, fatigue and pain. Thus, parents judge impairments by comparison to the child’s level of pre-injury functioning and taking into consideration environmental expectations. For example, if a child is back home and at school, academic and cognitive functioning might be rated moderately impaired by the parents because of the increased amount of academic tasks, despite objective improvements that had allowed the child to be discharged from rehabilitation and sent back to school.

In contrast to the GOS-Peds and PIFOS scores, the BRIEF and CBCL scores showed no significant improvement between 3 and 24 months, which suggests that these more specific questionnaires might not be the best way to assess longitudinal improvement (at least with the total scores). Indeed, executive and behavioural deficits might improve over time, although

they can also appear/worsen after a long delay post-injury [5,7], especially when environmental expectations increase. Given that parents answer using a combination of their knowledge of their child's pre-injury functioning and the child's current everyday life impairments, in the context of personal factors, these questionnaire-based ratings reflect more than an actual level of deficit [26,40,41].

Our findings also highlight the multi-dimensional nature of TBI outcomes and subsequent recovery as well as the high variability between participants and the heterogeneous patterns of recovery of different functional areas for the same patient. Despite an initial rapid recovery, subsequent functional outcomes, measured with the PIFOS, showed little and non-significant recovery beyond 12 months post-injury, with persistent limitations in patient's everyday life in a number of domains. The most impaired domains at 12 and 24 months post-injury were the social-emotional, cognitive-academic and physical domains (including very frequent and disabling symptoms such as pain and fatigue, which are frequently under-studied). Thus, our results indicate that the improvement noted in psychometric measures does not necessarily translate into functional improvements in daily settings [14] and highlight the importance of multimodal functional outcome assessment, as reported here.

More broadly, this study confirms the need for a combination of several outcome measures [20] to improve the practical scope and clinical significance of such cohort longitudinal studies.

Associated factors

Overall functional status was strongly correlated with a variety of concurrent factors over the first 24 months post-injury that were measured with various assessment means, combining clinician-rated, questionnaire-based, and situational (e.g., type of ongoing education) factors. Poorer functional outcome at 12 and 24 months was significantly associated with higher overall disability, presence of motor deficits and post-traumatic epilepsy, lower intellectual

ability, higher behavioural and executive function deficits, and poorer academic outcome at the same time points. These results indicate that the PIFOS appears to be an accurate and precise tool for determining and monitoring functional outcome, at least up to 24 months post-injury. Indeed, it is sensitive to change and highly correlated with objective clinical evaluation, neuropsychological tests, and proxy-reported questionnaires. As such, the PIFOS, based on a parent structured interview with a healthcare practitioner who knows the child's functioning, has the advantages of both subjective (questionnaire-based) and objective assessment tools, which allows for a more realistic and standardised assessment of outcomes, allowing to bypass a common limitation shared by many longitudinal pediatric studies.

Regarding early predicting factors of functional status, only initial injury severity factors (i.e., GCS, ISS and specifically length of coma) were significantly associated with functional outcome at each time point. Similar to prior studies [41], this severity effect was present despite the inclusion of all children with sustained severe TBI, which confirms that injury severity is a key predictor of outcome and persistent individual deficits in most domains [6,7,15,17] after childhood TBI.

Contrary to other studies (mostly investigating cognitive outcomes) [7,18,42–45], only pre-injury education difficulties were marginally associated with 12-month post-injury functional outcome. Other individual characteristics, sociodemographic variables and even age at injury were not significantly associated with functional outcome at 12 months post-injury. One explanation could be that functional outcome, as measured by the PIFOS, is based on the difference from pre-injury, which could help mask the pre-injury status effects. Additionally, the PIFOS covers larger domains of everyday functioning, which are influenced by a number of environmental factors that were not measured in the present study. Finally, the exclusion of the youngest children (<3 years at injury) might have contributed to the lack of effect of age at injury. A deeper understanding of the effects of age at injury will require more research,

combining imaging data and more restricted age-at-injury groups in larger samples. The too-often short duration of research studies hampers this effort because the changes in development expected to vary across ages at injury may not emerge at measurable magnitudes for some time.

Limitations

The current results should be interpreted taking certain limitations into account. Despite the large sample of children with severe TBI compared to previous studies, the overall sample size was small and the comparisons of children according to disability levels involved relatively small samples, which could have reduced the power of the analyses. Furthermore, the lack of a control group is a limitation, because a matched group of children with an orthopaedic injury could have been useful to determine the specific functional impairments due to the head injury and to control for the use of the PIFOS scale, especially at the latest time point (24 months post-injury), in that parents are asked to compare their child's abilities to the pre-injury performance. There could be a memory bias involved, and the child's ability 2 years previously was compared with the child's current ability, but progress in functional independence is expected to have occurred. Despite this limitation, the PIFOS scores, even at the latest time point, were highly correlated with severity indices and several concurrent outcomes, measured using performance-based tests, as well as parent-reported questionnaires. Parents may adapt their answers to the PIFOS items by using the child's pre-injury abilities but also the expected progress that should have occurred according to information for other children of a similar age. Also, at 12 and 24 months, the main complaints were in the social-emotional, cognitive-academic and physical domains (including pain and fatigue), which agrees with the frequently described sequelae of severe TBI, and parents would have picked up increased difficulties with school work, personality or behaviour.

Also, all patients underwent brain imaging at some point, but the data had not been centralised and combined, and analyses of relations between brain lesions and various outcomes was not possible.

Finally, we could not determine the effect of the rehabilitation therapies on outcomes because most children were hospitalised in a rehabilitation centre initially and received individually tailored multidisciplinary care that was maintained in the community after discharge when necessary.

Conclusion

This study adds to the literature an examination of the significant impact of childhood severe TBI on short- and medium-term clinical/neurological, functional outcome and overall disability level, with 4 of 5 children still showing moderate or severe disability at 2 years post-TBI, although with high variability among the group. These impairments were present despite a high level of initial and ongoing care/rehabilitation. Our results also illustrate the public health impact of childhood severe TBI, because a large proportion of those children experience long-lasting sequelae including negative socio-behavioural and cognitive outcomes, highly associated with disabling difficulties in academic performance, which also affects their participation, peer relationships and well-being. This study also highlighted the need for clinicians to provide careful evaluation and adequate follow-up for patients with severe TBI, during the first years after injury and beyond, in order to optimize the interventions and personalized care. A goal of future research will be to study longer-term outcomes, clarify the reasons for variability in recovery patterns among children with severe TBI and focus on the predictors, moderators, and mediators (including imaging and biomarker data) of long-term outcomes after pediatric severe TBI.

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Conflict of interest. None declared.

Legends

Figure 1. Flow-chart of the sample included in the study. PIFOS, Pediatric Injury Functional Outcome Scale

Figure 2. A) Glasgow Outcome Scale-Pediatric version (GOS-Peds). B) Mean scores on the Pediatric Injury Functional Outcome Scale (PIFOS) at 1, 3, 12 and 24 months post-injury.

Scores range from 0 (no change from pre-injury levels) to 4 (increasing need for support and limitations to daily activities). C) Full-Scale Intellectual Quotient (FSIQ) over time. Mean expected score in the general population = 100; < 85 (- 1 SD). D) Behavior Rating Inventory of Executive Functions (BRIEF): executive functioning in everyday life. Mean expected T-score in the general population = 50. Clinical cut-off score ≥ 65 (+1.5 SD). E) Child Behavior Checklist (CBCL): parent-rated everyday behaviour. Mean expected score in general population: T-score = 50. Clinical cut-off score ≥ 65 (+1.5 SD). * $p < 0.05$, ** $p < 0.01$; *** $p < 0.001$.

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Figure 1

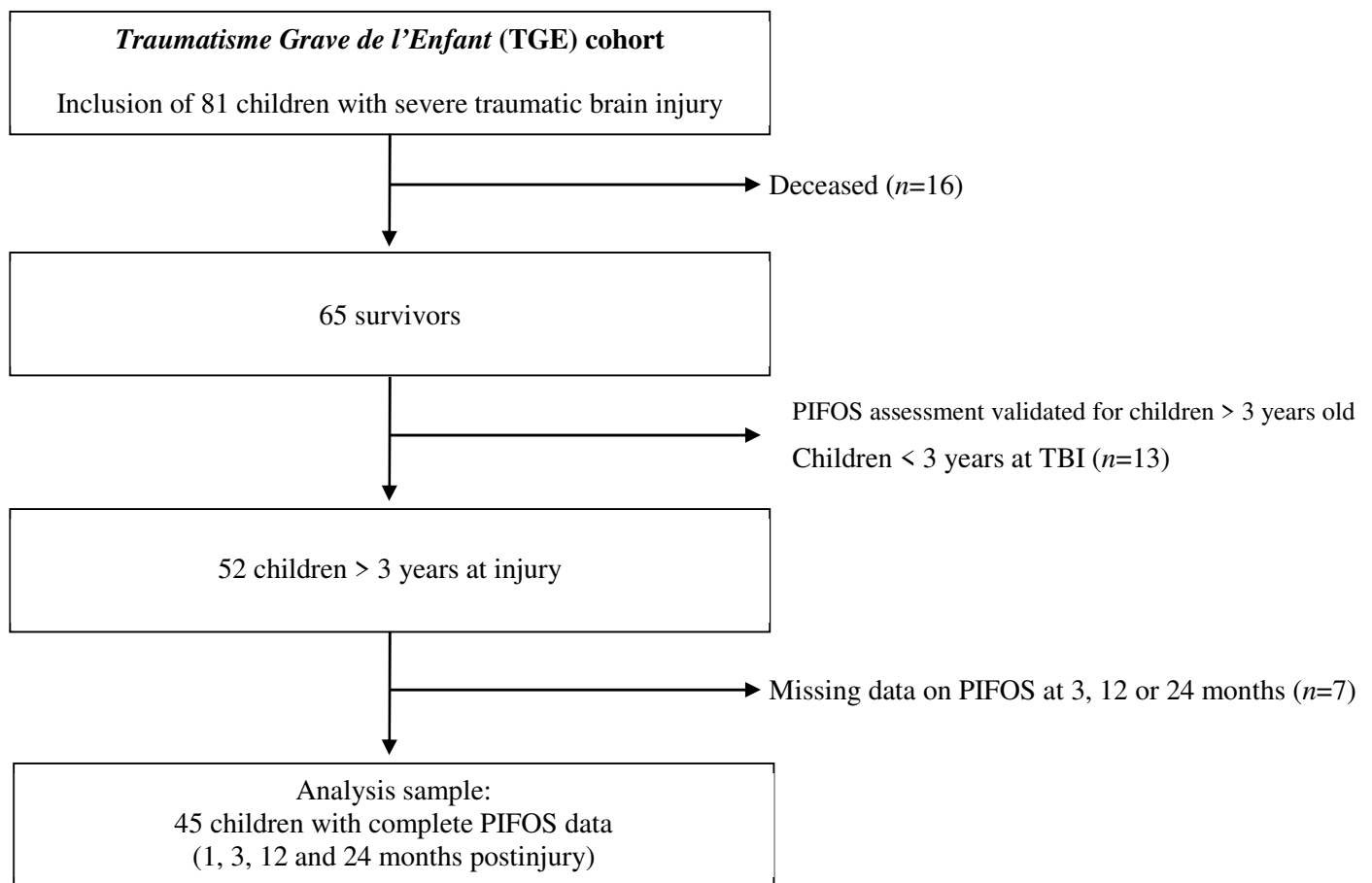
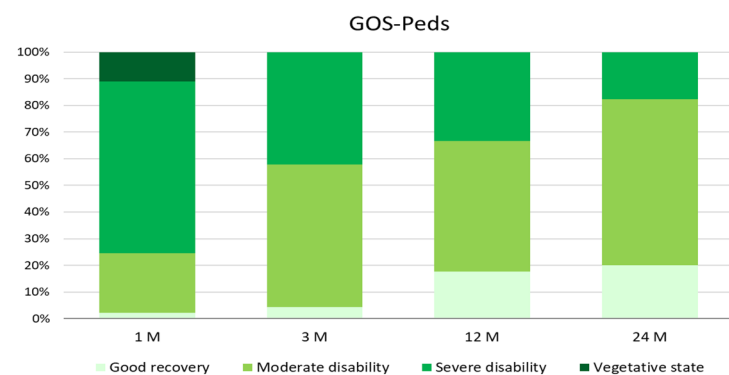


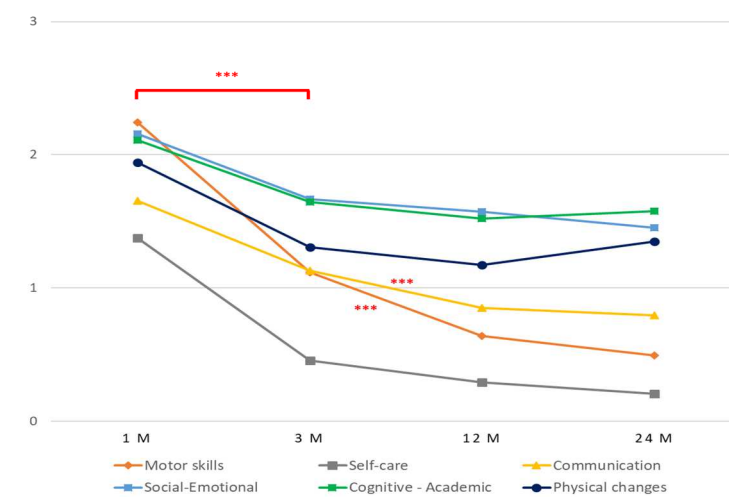
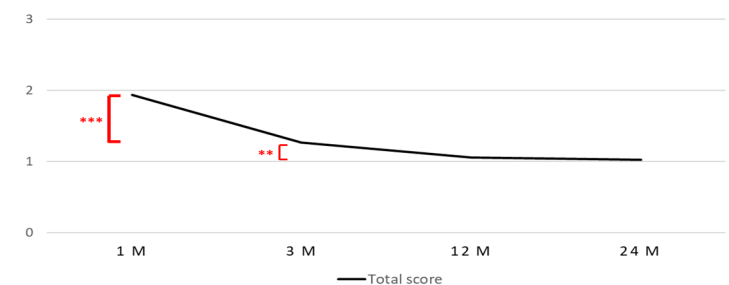
Figure 2

A.

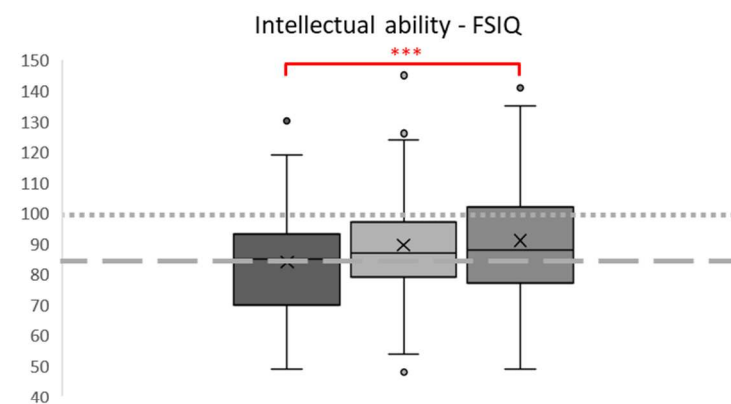


PIFOS

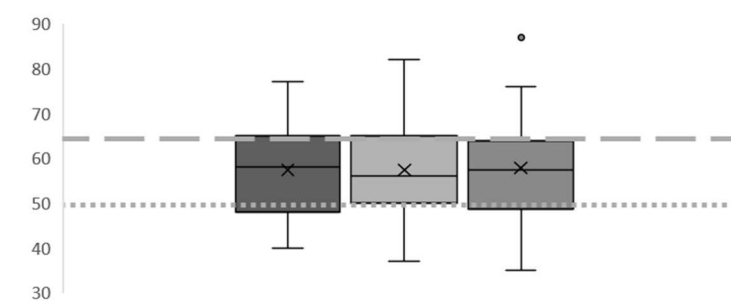
B.



C.

Executive function - BRIEF *GEC*

D.



Behavioural problems - CBCL

E.

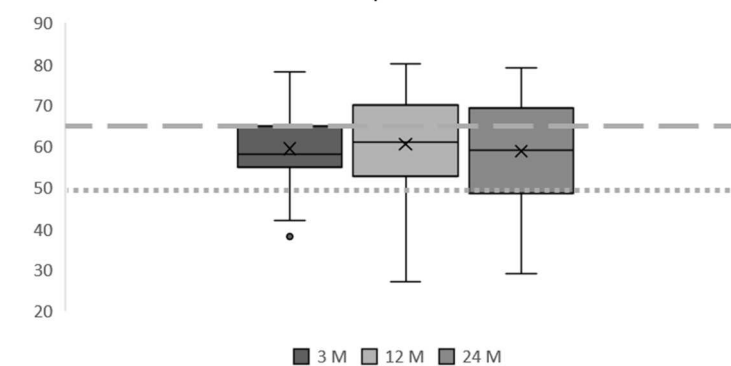


Table 1. Sociodemographic, initial injury severity and injury-related characteristics of the study participants (n=45).

		Min	Max
<i>Sociodemographic characteristics</i>			
Age at injury (years)	9.8 (3.5)	3.0	14.9
Sex, male n (%)	31 (69)		
Parental education level, n (%)			
Medium-high ^a	20 (44)		
Preinjury education, n (%)			
Assisted and/or delayed	11 (24)		
<i>Initial injury severity</i>			
Lowest Glasgow Coma Scale Score	6.2 (1.8)	3	9
Pediatric Trauma Score	4.4 (2.3)	-1	9
Injury Severity Score	27.1 (9.3)	4	50
Length of coma (days)	6.6 (4.8)	1	22
<i>Injury-related characteristics</i>			
Intracranial hypertension (yes), n (%)	12 (27)		
Brain hypo perfusion (yes), n (%)	34 (76)		
Collapsus (yes), n (%)	4 (9)		
Seizures (yes), n (%)	3 (7)		
Penetrating skull fracture (yes), n (%)	7 (16)		

Data are mean (SD) unless otherwise indicated.

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

Table 2. Clinical recovery and outcomes of the study participants at 1, 3, 12 and 24 months after severe traumatic brain injury (TBI).

	1 month		3 months		12 months		24 months	
Clinical impairments								
<i>Consciousness</i>								
Vegetative state	5	(11)	-		-		-	
Not able (or difficulties) to follow simple commands	12	(27)	2	(4)	1	(2)	-	
<i>Post-traumatic epilepsy</i>	0	(0)	1	(2)	3	(7)	3	(7)
<i>Locomotor disability</i>								
Motor deficits	21	(47)	17	(38)	12	(27)	5	(11)
Hemiplegia/cerebellar signs	15/16	(33)/(36)	10/16	(22)/(36)	4/11	(9)/(24)	3/4	(7)/(9)
Walking								
Walks with/without technical device	8/18	(18)/(40)	7/35	(16)/(78)	3/42	(7)/(93)	3/42	(7)/(93)
Dependent for locomotion	19	(42)	3	(7)	0		0	
<i>Sensory deficits</i>								
Somatosensory symptoms	3	(7)	4	(9)	2	(4)	2	(4)
Visual impairment	9	(20)	4	(9)	4	(9)	4	(9)
<i>Oral feeding impairment</i>	12	(27)	2	(4)				
Texture adaptation/feeding tubes	8/4	(18)/(9)	2/-	(4)/-	-		-	
<i>Sphincter control</i>								
Urinary/faecal incontinence	13/13	(29)/(29)	4/3	(9)/(7)	4/-	(9)/-	2/-	(4)/-
Ongoing medical management								
Pharmacological medication								
Antiepileptic/antispasmodic	1/8	(2)/(18)	2/3	(4)/(7)	3/1	(7)/(2)	3/1	(7)/(2)

Rehabilitation therapies							
Speech-language therapy	-	-	30	(67)	26	(58)	
Occupational therapy	-	-	19	(42)	15	(33)	
Physiotherapy	-	-	13	(29)	8	(18)	
Psychomotricity *	-	-	11	(24)	8	(18)	
Psychologist/psychiatrist			19/9	(42)/(20)	11/7	(24)/(16)	
Ongoing education							
Mainstream school			27	(61)	31	(70)	
With adaptation and/or grade retention			10	(23)	15	(34)	
Specialized education			17	(39)	12	(27)	
Within the rehabilitation department			13	(30)	4	(9)	
Special education institute			4	(9)	8	(18)	
<i>Missing information</i>			<i>1</i>		<i>1</i>		

* Psychomotricity is a healthcare profession well established in France. Psychomotor therapists receive training in psychological and cognitive domains as well as motricity (overall motricity, fine motricity, writing, bimanual co-ordination). They deal with the perception of the body in space, attentional disorders, co-ordination disorders and cognitive disorders. They can work with patients and their families in various environments such as neonatal intensive care unit, adult or children neurology or rehabilitation departments, and geriatric populations.

Table 3. Factors associated with functional outcome (total score of the Pediatric Injury Functional Outcome Scale [PIFOS]) at 1, 3, 12 and 24 months after severe TBI.

	1 month			3 months			12 months			24 months		
	<i>n</i>	<i>r</i>	<i>P value</i>	<i>n</i>	<i>r</i>	<i>P value</i>	<i>n</i>	<i>r</i>	<i>P value</i>	<i>n</i>	<i>r</i>	<i>P value</i>
Initial injury severity												
Age at injury	45	.27	0.07	45	.22	0.15	45	.08	0.60	45	.06	0.72
Lowest GCS Score	45	-.31	0.04	45	-.27	0.08	45	-.31	0.04	45	-.41	0.006
Pediatric Trauma Score	45	-.16	0.31	45	-.17	0.27	45	-.24	0.12	45	-.21	0.17
Injury Severity Score	45	.56	<0.0001	45	.49	0.0007	45	.44	0.003	45	.41	0.005
Length of coma	45	.72	<0.0001	45	.72	<0.0001	45	.62	<0.0001	45	.59	<0.0001
Postinjury outcomes												
<i>Clinician-rated outcomes</i>												
Overall disability (GOS-Peds)	45	.77	<0.0001	45	.74	<0.0001	45	.73	<0.0001	45	.76	<0.0001
Motor deficits [†]	45		<0.0001	45		<0.0001	45		<0.0001	45		0.02
Epilepsy [†]	-	-	-	45		0.04	45		0.0001	45		<0.0001
<i>Performance-based outcomes</i>												
Ongoing education [†]	-	-	-	-	-	-	44		0.0001	41		0.03
Intellectual ability												
FSIQ	-	-	-	42	-.64	<0.0001	44	-.64	<0.0001	43	-.54	0.0002
<i>Questionnaire-based outcomes</i>												
Executive Function												
BRIEF GEC	-	-	-	25	.52	0.008	30	.63	0.0002	32	.51	0.003

Behaviour

CBCL Total Problems	-	-	-	31	.45	0.012	34	.58	0.0003	28	.64	0.0003
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[†] Student's *t*-test; *r*, Pearson correlation coefficient; *ns*, non-significant; GCS, Glasgow Coma Scale; GOS Peds, Pediatric Glasgow Outcome Scale; FSIQ, Full Scale Intellectual Quotient; BRIEF, Behavior Rating Inventory of Executive Function; GEC, Global Executive Composite; CBCL, Child Behavior Checklist.