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**Executive functions and attention 7 years after severe childhood traumatic brain injury:
results of the Traumatisme Grave de l'Enfant (TGE) cohort**

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Abstract

Objectives: Severe childhood traumatic brain injury (TBI) leads to long-standing executive function and attention deficits, with negative consequences for participation, academic outcome and independence. This study aimed to assess executive function and attention 7 years after severe childhood TBI in comparison with a matched control group and to investigate associated factors.

Methods: Children (<15 years) with severe accidental TBI consecutively admitted in a single trauma center over 3 years were included in the Traumatisme Grave de l'Enfant (TGE) prospective longitudinal study. Of the 81 children initially included, 65 survived. At 7 years post-TBI, executive functions and attention were assessed in 27 participants (42% of the 65 survivors) by using a combination of computerized tasks from the Test of Attentional Performance (TAP) and the Behavioral Rating of Executive Functions (BRIEF) questionnaire. Patients were compared to a group of 27 typically developing controls who were matched for sex, age and parental education level.

Results: Among the 27 participants, mean (SD) age at injury was 7.7 (4.6) years, and mean length of coma 5.6 (4.6) days. Regarding the TAP, the number of errors was significantly higher ($p = 0.003$) and reaction time marginally slower ($p = 0.08$) in the TBI than control group. The BRIEF questionnaire completed by parents indicated significantly more executive difficulties in the TBI than control group (Behavior Regulation Index, $p = 0.005$; Metacognitive index, $p = 0.02$; Global Executive Composite, $p = 0.012$). Correlations between BRIEF and TAP scores did not reach statistical significance. BRIEF total score was correlated moderately with length of coma ($r = 0.40$, $p = 0.037$), and TAP scores were correlated with the Full-Scale Intellectual Quotient (total number of errors: $r = -0.48$; $p = 0.01$; mean reaction time: $r = -0.51$; $p = 0.009$).

Conclusions: Executive and attention deficits were evident 7 years after severe childhood TBI. Computerized tasks and questionnaires provide complementary and non-redundant information. Systematic long-term follow-up should be provided until the transition to adulthood, to assess ongoing development and to implement timely tailored interventions.

Keywords: severe traumatic brain injury; child; adolescent; long-term outcome; executive functions

Introduction

Traumatic brain injury (TBI) is the leading cause of childhood and adolescent death and lifelong acquired disability [1]. Severe TBI is defined by a Glasgow Coma Scale (GCS) score 3 to 8, the presence of altered consciousness beyond the first 24 hr after the injury, and/or the presence of post-traumatic amnesia ≥ 7 days. Lesions observed on brain imaging may also contribute to the classification of TBI severity [2]. Severe TBI represents only 3% to 7% of all TBIs [3], but most individuals with severe childhood TBI will have persistent secondary disability [1], with frequently altered cognitive, emotional, behavioral and psychological functions, affecting academic achievement [4], overall independence, participation [5], and quality of life [6]. Among the cognitive deficits after childhood TBI, executive function (EF) deficits are frequent and contribute greatly to overall impairments in everyday home and school environments [4,7].

EFs are defined as a collection of related but distinct cognitive abilities that allow individuals to engage efficiently and effectively in intentional, complex, and purposeful goal-directed problem-solving actions, through conscious and effortful processing [8]. EFs are involved in planning, problem solving, concept formation, action monitoring and mental flexibility. They allow the adaptation to novel situations, especially when action routines and

over-learned sequences are not sufficient [8,9] and play an important role in everyday life, independence and academic achievement [4].

EFs are thought to be mediated by the frontal and prefrontal regions; however, the integrity of the whole brain is required for intact executive functioning [9]. Brain lesions occurring after severe TBI can disrupt brain maturation and future skills development [7]. Indeed, EFs are immature during childhood and follow extended maturation from infancy to late adolescence [10]. Diamond's model of EF development postulates the existence of 3 central EFs — inhibition, working memory, and cognitive flexibility — which have mutual influences throughout development and constitute the foundations for the subsequent development of more complex EFs, such as planning, problem solving and reasoning [10].

Attentional capacities are related to EF (e.g., working memory involves attention and is included in EF), but they are generally considered distinct. They can be classified in 3 functional components: *alerting*, which allows for being vigilant to a stimulus; *orienting*, for selecting useful information during multiple solicitation; and *executive control* [11]. Van Zomerén and Brouwer differentiate attention into 2 competencies: *selectivity* and *intensity*. *Selectivity* includes *focalized attention* with inhibition of distractors and *divided attention*, which allows for the performance of 2 tasks simultaneously. *Intensity* consists of *sustained attention* allowing to maintain attention levels over prolonged periods of time, and *alert*, which is the ability to mobilize attentional resources in response to an alert signal [12].

Assessment of EF and attention is challenging, because standard neuropsychological “performance-based” tests do not always predict impairments in everyday life activities, and their ecological validity has been questioned [13]. Therefore, combining standard neuropsychological tests with more ecological assessments (e.g., questionnaires) is recommended and thought to better reflect the impact of EF deficits in patients' daily life. For instance, EF deficits in everyday life after childhood TBI were frequently observed by use of

the Behavior Rating Inventory of Executive Functions (BRIEF) questionnaire [13]. This questionnaire, described in further detail in the Methods section, assesses different aspects of EF (e.g., planning, shift, organization, behavioral regulation) impacting daily life. Moreover, previous investigations and a review of 20 studies of children and adults using different assessment tools aimed at assessing EF have reported the lack of correlation between neuropsychological test scores and questionnaire scores, which seem to assess different aspects of EF [13,14].

In studies of EF and attention after childhood TBI, severe TBI is underrepresented, with greater emphasis on milder injuries [7]. Overall, EF deficits are frequently reported following severe TBI [15]; however results are not always consistent, probably because of the diversity of ages at assessment and injury, TBI severity and assessment tools. As previously noted, results can vary depending on the assessment tools used to assess EF (i.e., neuropsychological tests or questionnaires). In addition, results might be different in children versus adults, given the late maturation of the prefrontal cortex and the extended postnatal development of EF and attentional abilities.

Deficits in goal setting and processing speed [16,17], inhibition [18,19] and working memory [18,20] have been reported, but findings seem less consistent for deficits in planning and flexibility [16–18]. These discrepancies may be explained by multiple factors (e.g., assessment tools, injury severity, age at injury and assessment, age of acquisition of the corresponding skills, time since injury, other family- and child-related factors), whose effects are difficult to disentangle in relatively small samples of patients with severe TBI. Other studies have reported deficits in attentional capacities after childhood TBI [19] as well as recovery of attentional capacities in the long term after severe TBI [17,20].

Many child-level and injury-related factors have been associated with the presence and severity of attention/EF deficits after childhood TBI, including pre-injury abilities [21], TBI

severity [16,18,22] and age at injury [18,23]. In addition, difficulties in post-injury attention/EF skills have been linked to family environmental factors, such as low parental socioeconomic status (SES) [18,24], poor family functioning [25] and authoritarian parenting styles [26], which underlines the importance of considering the role of environmental factors in studies investigating the effect of early severe TBI on long-term attention and EF.

In the initial phase of the prospective longitudinal study reported here (Traumatisme Grave de l'Enfant [TGE] — Severe Childhood Trauma), EF was assessed at 3, 12 and 24 months post-injury by using a combination of neuropsychological standardized tests and the BRIEF questionnaire [18]. The results indicated significant impairment of working memory, inhibition, and attention assessed by the BRIEF questionnaire, with little or no recovery at 24 months after TBI, according to the evolution of individual scores over time from 3 to 24 months. Performance-based EFs (i.e., exclusively results of the neuropsychological tests for each EF domain) were significantly impaired at 3 months but improved to normal by 12 months. EF performance was significantly affected by parental education, TBI severity and age at injury [18]. These results agree with the findings from the above-mentioned studies and underline the discrepancies observed in attention and EF skills when using performance-based instruments (i.e., neuropsychological tests) and questionnaire-based assessments.

The current study aimed at extending the findings from the previous longitudinal follow-up times with an investigation of the same sample at 7-year follow-up. Thus, the primary aim was to investigate EFs and attention at 7 years after severe childhood TBI in comparison with a control group matched for sex, age and parental education level, by using a combination of performance-based neuropsychological tests and an ecological measure (parent-rated questionnaire assessing everyday EF). Secondary aims were to 1) investigate the factors associated with long-term EF and attention deficits and 2) explore the relation between performance- and questionnaire-based assessments of EF.

For the first aim, we hypothesized lower levels of EF and attention in the TBI group versus controls. For the secondary aim, we hypothesized 1) worse executive and attention performance associated with increased injury severity, young age at injury, low parental education level and poor family functioning, and concurrent outcome measures at 7 years post-TBI and 2) weak correlations between performance- and questionnaire-based assessments of EF, with possibly different factors related to each of these types of assessments.

Materials and methods

The present work is part of a larger prospective longitudinal study (TGE) aimed at determining overall (e.g., current situation, academic achievement and independence, overall disability, intellectual ability) and specific outcomes (e.g., attention skills, EF, memory, behavioral difficulties, participation, fatigue) after severe accidental childhood TBI sustained before age 16 years (for a detailed description of recruitment and sample constitution, see [18,27,28]).

Participants

In total, 81 children with severe childhood TBI consecutively admitted in the pediatric neurosurgical intensive care unit (ICU) of Necker-Enfants-Malades Hospital in Paris at the acute stage of TBI were included. All children presented the criteria for severe TBI. Of these, 65 children (80%) survived and 39/65 (60%) agreed to participate in the 7-year post-TBI follow-up. The remaining 26 survivors were lost to follow-up or refused to participate. Participants ($n=39$) and non-participants ($n=26$) did not differ in socio-demographic background, initial injury severity, injury-related characteristics or 1-year post-injury outcomes, including Full-Scale Intellectual Quotient (FSIQ) and BRIEF scores ($p>0.05$ for all).

Among the 39 participants followed for 7 years post-TBI, 27 (42% of the 65 survivors) had available data on both performance- and questionnaire-based measures of EF. The remaining 12 participants had neuropsychological or BRIEF questionnaire data but not both assessments. These incomplete assessments were due to inability/refusal to perform the assessments and/or return/respond to questionnaires. Therefore, the analysis sample consisted of 27 participants who were followed longitudinally for 7 years after severe pediatric TBI.

A population-based group of 38 healthy controls was recruited from local schools or through general medical practices at the 7-year follow-up. Controls were closely matched to participants in the TBI group for age (± 3 months), sex and parental education (± 2 years' education). From this control group, 27 participants had available data on both performance- and questionnaire-based measures of EF and were considered for the present analyses. Despite the matching procedure between participants with TBI and controls, some patient-control dyads had incomplete data on performance- and/or questionnaire-based measures.

Measures

Initial injury severity was assessed by the Glasgow Coma Scale (GCS) [29], the Pediatric Trauma Score ([PTS]; range -6 to +12, lower scores indicate more severe injury) [30], and the Injury Severity Score ([ISS]; range 0 to 75, higher scores indicate greater severity) [31], and length of coma (in days). Initial injury-related characteristics were also recorded: absence or presence of intracranial hypertension, brain hypo-perfusion, collapsus, seizures and penetrating skull fractures.

Outcomes at 1 year post-TBI

To assess the overall level of disability and functional outcome 1-year post-injury, we used the Glasgow Outcome Scale modified for children (GOS-Peds) [32] and the Pediatric Injury

Functional Outcome Scale (PIFOS) [33]. The presence of post-traumatic epilepsy and motor deficits at 1 year post-TBI were also recorded.

Outcomes at 7 years post-TBI

Standardized neuropsychological tests of attention and executive functioning:

We used 3 developmentally-appropriate subtests of the Test of Attentional Performance (TAP) computerized battery, assessing visual, auditory and divided attention, flexibility and inhibition [34]. Outcome measures included reaction times and errors (e.g., omissions, false alarms). Previous studies have underlined the psychometric soundness of the subtests in this testing battery in relation to the subcomponents of attentional processes in child and adult TBI [35,36]. However, to our knowledge, a global score for attentional skills has not been proposed in previous investigations, and analyses tend to be performed separately for each of the subtests assessing the subcomponents of attention.

To assess planning and multitasking ability, the Errands Test was used in patients ≥ 16 years old [37], and the Six-part subtest of the Behavioural Assessment of the Dysexecutive Syndrome for Children (BADSC) was used for children < 16 years old [38]. Finally, to assess Working Memory, we used the Working Memory Index of the Wechsler Intelligence Scales [39,40].

Questionnaire-based rating of everyday executive functioning: We used parent/proxy reports of age-appropriate versions of the French adaptation and standardization of the BRIEF questionnaire [41], which consists of 8 clinically and theoretically driven subscales measuring different aspects of EF, yielding 2 composite indices: Behavioral Regulation Index ([BRI]: subscales Inhibition, Shift, Emotional Control) and Metacognitive Index ([MI]: subscales Initiation, Working Memory, Plan/Organize, Organization of Materials and Monitor). The Global Executive Composite (GEC) index provides an overall measure of EF. Results are expressed as *T*-scores (mean [SD]=50 [10]), with higher scores indicating worse functioning.

Concurrent outcomes at 7 years post-TBI

Epilepsy and motor deficits (presence vs absence of motor deficit and/or signs of cerebellar dysfunction) were recorded upon medical neurological examination.

Type of ongoing education was coded as mainstream education (with or without help/adaptations) versus special education.

Overall disability was assessed with the Glasgow Outcome Scale-Extended Pediatric Version (GOS-E Peds) for up to age 17 years [32] and with the GOS-E for adults [42]. Overall outcome was classified into 3 levels: good recovery, moderate and severe disability.

Behavior problems were evaluated with parent-report forms of the Child Behavior Checklist (CBCL) and the Adult Behavior Checklist (ABCL), as well as self-report forms of the Youth Self-Report (YSR) and the Adult Self-Report (ASR) [43–45]. Three age-standardized summary *T*-scores (mean [SD]=50 [10]) were used as outcome measures: Internalizing problems (e.g., anxiety, depression), Externalizing problems (e.g., aggressiveness, agitation, impulsivity) and Total problems, with higher scores reflecting more behavior problems.

Health-related quality of life (HRQoL) was assessed with age-appropriate French-validated versions of self- and parent/proxy-report forms of the Pediatric Quality of Life Inventory (PedsQL) for children (age 2-18 years) [46] and young adults (age 18-25 years) [47], with higher scores indicating better HRQoL

Fatigue was assessed with the self- and parent-report forms of the Multidimensional Fatigue Scale (MFS) for children (age 2-18 years) [48] and young adults (age 18-25 years) [49], with higher scores indicating lower fatigue levels.

Family functioning was assessed with the French versions of the 12-item short-form from the Family Assessment Device (FAD) [50], with higher scores indicating poorer family functioning.

Intellectual ability was assessed with age-appropriate French versions of the Wechsler

Intelligence scales, specifically the Wechsler Intelligence Scale for Children-IV and the Wechsler Adult Intelligence Scale-IV [39,40].

Procedure

The TGE study was initiated at the Paris 5 University Hospital Necker-Enfants-Malades and conducted in the Rehabilitation Department for Children with Acquired Neurological Injury in the Saint Maurice Hospitals. The current study was approved by the ethics committee of the Comité de Protection de Personnes d'Île-de-France VI (CPP IDF VI) and all parents and/or patients gave their informed written consent. The assessments included a medical/neurological examination and a comprehensive neuropsychological assessment. The reporting of the present work follows the guidelines proposed in the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement [51].

Statistical analysis

Data analyses were conducted with SAS v9. First, we used univariate procedures (Student *t* test) to compare patients and controls at 7-year follow-up according to EFs, intellectual ability, behavior, HRQoL, fatigue and family functioning. To reduce the number of comparisons, we computed 2 global scores for the TAP. We calculated a Reaction Time (RT) total score by averaging the mean reaction times on all subtests of visual and auditory attention, dual task, flexibility and inhibition, and an Errors Total score by averaging the number of false alarms, omissions and errors on all subtests. This option was justified by the significant correlations between RTs for the different subtests as well as between the number of errors among the several subtests. The reliability indices obtained for these global scores supported this option, with Cronbach reliability coefficients in the acceptable range for the RT and Errors Total score ($\alpha=0.89$ and 0.86 , respectively, for participants with TBI; $\alpha= 0.93$ and 0.75 , respectively, for controls).

In a second set of analyses, we focused on participants with severe TBI. We used univariate procedures (Student *t* test, Pearson correlation coefficient, ANOVA) to examine the associations between initial injury severity, injury-related characteristics and post-injury outcomes at 1 and 7 years after TBI. Because age was significantly associated with performance on the TAP, we controlled for age on all procedures examining associations with TAP scores. Statistical significance was set at $p < 0.05$.

Results

Study participants

Table 1 describes the socio-demographic characteristics of the TBI ($n=27$) and control ($n=27$) groups, the injury initial characteristics for the participants in the TBI group, and 1- and 7-year post-injury outcomes. One-third of participants had reached adult age (>18 years) at 7 years post-injury. Overall, 18% of participants at 1 year post-injury and 62% at 7 years post-injury showed good recovery according to the GOS/GOS-E.

Clinical impairments in the TBI sample at 7 years post-injury

Five participants (19%) presented a severe overall disability according to the GOS, 6 (22%) presented motor deficits, 2 (7%) epilepsy, and 3 (11%) were enrolled in special education institutions. FSIQ was < 70 for 1 (4%) participant and < 80 for 8 (31%) participants. For 5 (19%) participants with TBI, the number of errors in the TAP was higher than the highest score (15.9) observed in the control group, and for 2 (7%), the RT was higher (slower) than the highest scores observed in the control group (942.8).

For the questionnaires, the EF global scores (BRIEF GEC) were above the proposed clinical cut-off for 12 (44%) participants. The proportion of participants with TBI with scores above (behavior problems) or below (HRQoL and fatigue) the proposed clinical cut-off scores were 33% for parent-reported total behavioral problems, 26% for self-reported total behavioral

problems, 26% for parent-reported HRQoL, 23% for self-reported HRQoL, 53% for parent-reported fatigue; and 54% for self-reported fatigue.

Comparisons between participants with TBI at 7 years post-injury and controls

TAP results (Table 2)

As compared with controls, participants with TBI showed significantly ($p < 0.05$) poorer performance on 6 of the 12 outcome measures of visual, auditory and divided attention, mainly those measuring false alarms and omissions. Regarding flexibility, patients made significantly more errors than controls on the Digit and Letters task. Performance on the Inhibition subtest did not significantly differ between the groups. The total number of errors was significantly higher in the TBI group than controls ($p = 0.003$) and participants with TBI showed overall slower mean reaction time than controls although not significantly ($p = 0.08$).

Errands Test and Six-part Test (Table 2)

The groups did not differ in total number of errors of the Errands Test or the standard score of the Six-part test.

BRIEF questionnaire (Table 3)

All subscale scores and composite indices (except the Initiate and Organization of materials subscales) were significantly higher (e.g., worse executive functioning) for the TBI than control group. For example, only 4 (15%) control participants had scores above the clinical cut-off (≥ 65), whereas 12 (44%) participants in the TBI group had scores in the clinical range (chi-square=5.68, $df=1$, $p = 0.017$).

Concurrent outcomes at 7 years post-TBI (Table 4)

As compared with controls, the TBI group had significantly lower FSIQ score (Table 2), more behavior problems and higher fatigue levels according to parental reports, as well as lower HRQoL, more externalizing difficulties and higher fatigue levels according to self-reports. The family functioning score (parent-report) was similar in the 2 groups.

Association of EF and attention with socio-demographic factors, injury-related characteristics and 1-year post-injury outcomes

TAP

Higher (worse) global RT score and Total Errors were correlated with younger age at follow-up ($r = -0.47, p = 0.013$ and $r = -0.70, p < 0.001$, respectively). We controlled for age on all the statistical procedures described below.

Slower reaction time was significantly associated with outcomes assessed at 1 year post-injury, namely, presence of epilepsy ($F(1,26)=11.2, p = 0.003$) and lower functional outcome score ([PIFOS], $r = 0.51, p = 0.012$). No other significant associations were observed between the TAP scores and socio-demographic, initial injury severity or injury-related characteristics.

BRIEF questionnaire

High (worse) BRIEF GEC score was moderately correlated with length of coma ($r = 0.40, p = 0.037$) and poor functional outcome score (PIFOS) at 1 year post-injury ($r = 0.53, p = 0.009$). No other correlation was found between the BRIEF GEC and any socio-demographic factors, injury severity, age at injury, or injury-related characteristics ($p > 0.05$, in all cases).

Association of EF and attention with concurrent outcomes assessed at 7 years post-injury

TAP

Slow RT score was significantly associated with presence of epilepsy ($F(1,26)=11.7, p = 0.003$) and enrollment in special education at 7 years post-injury ($F(1,26)=4.5, p = 0.045$). It was significantly correlated with poor self-reported HRQoL and low FSIQ (Table 5). The association between RT Total score and self-reported HRQoL was no longer significant when the effects of FSIQ were controlled for.

High Total number of Errors was significantly correlated with low FSIQ, poor parent-reported HRQoL, more parent-reported behavioral problems (Externalizing and Total problems) and more self-reported behavioral problems (Externalizing problems) (Table 5).

BRIEF questionnaire

Parental reports of impairments in EF (GEC) were significantly and often strongly associated with all other questionnaire-based parental reports, in the expected direction: more behavior problems, reduced HRQoL, increased fatigue, and poor family functioning (Table 5). Correlations with self-reports were moderate and in general not significant.

Associations between tasks and questionnaire evaluating EF and attention at 7 years post-injury

Correlations of total errors and mean RT of the TAP with the BRIEF scores were in the expected positive direction but did not reach statistical significance (Errors and mean RT with GEC: $r = 0.33, p = 0.097$ and $r = 0.34, p = 0.094$; with BRI: $r = 0.33, p = 0.096$ and $r = 0.33, p = 0.101$; with MI: $r = 0.28, p = 0.164$ and $r = 0.30, p = 0.139$).

Discussion

The present findings reveal significant deficits in EF and attention, measured by computerized tests and the BRIEF questionnaire, at 7 years after severe childhood TBI. In the performance-based neuropsychological tests, simple auditory attention, divided attention and flexibility were the most impaired, whereas visual attention and inhibition subtest scores did not differ between children with TBI and controls. However, the number of errors in the TAP tended to be systematically higher in patients than controls and the non-significance of some results could be in part due to lack of statistical power.

According to parental reports regarding their child's EF, difficulties were even more pronounced in the TBI group, with differences between groups close to 1 SD, representing large effects. Regarding factors associated with EF at 7 years post-injury, both performance test scores and the BRIEF score showed some weak associations with markers of injury severity and/or functional impairment at 1 year post-injury. Performance-based test scores but not the BRIEF score were correlated moderately with FSIQ. However, the BRIEF parent-report score was correlated moderately or strongly with other parental report scores assessing behaviour, fatigue, quality of life, and family functioning. As expected, scores for standardised tests and questionnaires assessing EF were poorly correlated. Finally, as previously reported, our study also highlighted the presence of significant behavioural difficulties, fatigue and low quality of life after severe childhood TBI [6,27,52].

These findings confirm previous studies reporting EF deficits in the short and long term [15,20,23] after childhood TBI, although in some studies, long-term deficits were not always significant, possibly because of the low number of participants with severe TBI [16,53,54]. For instance, Mangeot et al. [53] reported higher rates of EF deficits by using the BRIEF questionnaire in severe and moderate TBI groups at 5 years post-injury, whereas Anderson et al. [54] did not find statistically significant differences at 10 years post-injury in

BRIEF score between the TBI and control groups, regardless of injury severity. However, the severe TBI group ($n=19$) tended to have worse GEC scores than the control group.

Previous studies of executive skills after childhood TBI have reported persistent impairments of inhibition [55] and working memory [56], whereas flexibility and planning [20] seem to be more robust to the effects of TBI [18,57]. This finding could be explained by the protracted development of flexibility and planning, whose impairments might not be apparent initially and emerge over time [7,58].

Our study highlighted significant long-term working memory impairments, evident in standardized tests as well as in the BRIEF questionnaire, consistent with previous studies (for a review, see [56]) and with results of follow-up of the TGE cohort during the first 2 years post-injury [18]. Regarding inhibition, results were less consistent, with a lack of difference between groups in the TAP inhibition subtest, in contrast with significant inhibition impairments with the BRIEF questionnaire, which suggests inhibition deficits in everyday life. The present findings show deficits in flexibility, in standardized tests as well as everyday life, similar to a study of a younger age group at 5 years post-injury [16], but contrary to another report [17].

Regarding planning and multitasking, our results contrasted, with no differences between groups in the neuropsychological tests as compared with impairments in the BRIEF questionnaire. The Errands Test and Six-part test, used to assess multitasking, had to be performed in smaller age groups, which might have reduced the analysis power. Furthermore, the mean standard score of 8.4 on the Six-part test in the TBI group was similar to that in various studies using this test for patients with TBI or other acquired brain injury [13,59]. However, this score did not significantly differ from that for the control group (8.7), which could be due to the careful recruitment of the control group, with participants from very diverse backgrounds, including low SES. However, the scores of the control group on the Six-

part test contrast with their BRIEF scores, which were exactly in the expected normative range. In previous stages of this prospective longitudinal study, EF was assessed at 3, 12 and 24 months post-injury by using a combination of standardized tests and the BRIEF questionnaire [18]. The BRIEF score revealed significant impairment in working memory, inhibition, attention and global EF across time. However, for performance-based neuropsychological tests in general, children showed impairment at 3 months post-injury, but scores improved significantly to reach the normal range by 12 months. No impairment was found on planning at any time with the tests used.

Regarding attention, the results suggest persistent attention deficits after severe childhood TBI, especially for errors more than reaction time, as was previously reported [60,61], although not consistently [17]. Attention was not homogeneously impaired, with auditory attention and divided attention more impaired than visual selective attention, in accordance with the literature [62].

Although both performance- and questionnaire-based assessments of EF showed specific significant impairments, scores were not significantly correlated with each other, as is often reported in the literature [14]. This finding confirms that these 2 types of assessments are complementary and should be combined to provide a comprehensive assessment of EF [14].

At 7 years post-injury, factors associated with EF differed by type of assessment used. The TAP subtest composite scores was not related to initial severity indices but were associated with 1-year post-injury outcomes (i.e., post-traumatic epilepsy and worse functional status at 1-year post-injury), similar to findings of the earlier follow-up of the cohort [18]. TAP scores were also correlated with 7-year outcomes such as intellectual ability and type of ongoing education, which suggests the deleterious consequences of attention and EF deficits for academic achievement, as already reported [4]. However, the BRIEF GEC

score was only moderately correlated with severity indices (length of coma and 1-year functional outcome), which agrees with previous studies [16], but was highly correlated with concurrent parent-rated questionnaire-based outcomes (behavior, HRQoL, and fatigue), as previously reported [28].

Although we did not find an association of EFs with parental education, as opposed to earlier phases of the study [18], we found an association of the BRIEF GEC score with family functioning, measured by the FAD questionnaire, as previously reported [53]. Indeed, the quality of the family environment [63] and higher SES [24] have been reported to influence recovery after severe TBI. Finally, although several studies reported lower age at injury associated with worse EF outcomes [18,23], this was not confirmed in our study.

Parent- and self-reported externalizing problems were significantly associated with more total errors on the TAP. This finding suggests an influence of disruptive behaviors on performance-based assessments and provides a plausible explanation for the differences between groups in TAP performance, which might be related to higher rates of impulsive and disruptive behavior in individuals with TBI.

Finally, all parent-report questionnaire scores were significantly correlated with each other, whereas the parent BRIEF score was only marginally (or not) correlated with self-report questionnaire scores. Correlations between questionnaire scores are generally much higher when the questionnaires are answered by the same informant versus different informants [27]. This issue has been raised in previous studies using multiple questionnaires completed by the same informant. When all items of all the questionnaires have a positive/negative polarity, respondent-level factors and contextual factors may generate and strengthen the correlations between questionnaires aimed at assessing different constructs [64,65]. Self- and parent-reports, especially when assessing constructs such behavior, fatigue or quality of life should both be used, because they each collect unique information [66].

This study has some limitations. First, results are reported only for participants who had complete data on both the computerized assessment and BRIEF questionnaire, which reduced the number of available participants from 39 to 27. The limited sample size and lack of normative data for some age groups in some measures (e.g., TAP) hindered the statistical power of the present study. However, participants and non-participants did not differ in demographic and severity factors and cognitive and executive assessments performed at 3, 12 and 24 months. Second, the TAP battery lacked norms in some age groups, which led us to use only raw scores and adjust for age. Finally, although brain imaging was performed systematically, precise data collection was not performed for this study, which did not allow for analysis of relationships between EF performance and brain lesion characteristics.

In conclusion, cognitive and behavioral aspects of EF and attention were significantly impaired at 7 years after severe childhood TBI, with consequences for everyday life and academic achievement. The aspects were moderately related to initial TBI severity and 1-year functional outcome, post-traumatic epilepsy and family functioning. EF outcomes were associated with behavioral difficulties, health-related quality of life and fatigue, showing the deleterious effects of TBI severity across domains. This study has confirmed the challenges of assessing EF and the importance of combining both performance- and questionnaire-based measures for a comprehensive assessment [13], as well as the paramount importance of following survivors of childhood severe TBI in the long term. Regarding clinical implications, persistence of attention and executive deficits in the long term and their consequences require early systematic implementation of long-term specialized follow-up for all children and adolescents who sustained severe TBI. Special attention should be devoted to those who sustained the most severe injuries, who still exhibit significant functional impairments at 1-year post-injury, and who exhibit post-traumatic epilepsy. This follow-up should lead to implementation of timely, appropriate, tailored, validated interventions, in collaboration with

“everyday people” (*e.g.*, parents, teachers, school aids) [67,68]. Follow-up should be pursued until transition to adult services, which should be planned well in advance.

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Conflict of interest. None declared.

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Table 1. Sociodemographic, pre-injury education, and early traumatic brain injury characteristics of study participants (n=27).

Age at follow-up , mean (SD) (range)	15.6 (4.5) (8.6–22.7)
Boys , <i>n</i> (%)	16 (59)
Parental educational level , <i>n</i> (%)	
<i>Medium-high</i>	15 (57)
Pre-injury education , <i>n</i> (%)	
<i>Assisted and/or delayed</i>	3 (11)
Initial injury severity , mean (SD) (range)	
Age at injury	7.7 (4.6) (0.25–14.7)
Minimal Glasgow Coma Scale score	6 (1.7) (3–8)
Injury Severity Score	26.2 (9.6) (4–45)
Paediatric Trauma Score	4.2 (2.2) (0–9)
Length of coma (days)	5.6 (4.6) (1–22)
Injury-related characteristics	
Intracranial hypertension (yes), <i>n</i> (%)	6 (24)
Brain hypoperfusion (yes), <i>n</i> (%)	20 (80)
Collapsus (yes), <i>n</i> (%)	3 (11)
Seizures (yes), <i>n</i> (%)	2 (7)
Penetrating skull fracture (yes), <i>n</i> (%)	2 (7)

1-year post-injury outcome	
Overall disability (GOS-E Peds)	
<i>Good/moderate/severe, n (%)</i>	5 (18) / 15 (56) / 7 (26)
Motor deficits (presence), <i>n (%)</i>	10 (37)
Epilepsy (yes), <i>n (%)</i>	2 (7)
Functional outcome (PIFOS score) (<i>n=24</i>), mean (SD) (range)	24.9 (15.8) (4–65)
7-year post-injury outcome	
Overall disability (GOS-E Peds)	17 (62) / 5 (19) / 5 (19)
<i>Good/moderate/severe, n (%)</i>	
Motor deficits (presence), <i>n (%)</i>	6 (22)
Epilepsy (yes), <i>n (%)</i>	2 (7)
Ongoing education	
<i>Specialized, n (%)</i>	3 (11)

GOS-E Peds, Glasgow Outcome Scale-Extended, Pediatric version; PIFOS, Pediatric Injury

Functional

Outcome.

Table 2. Comparison of participants with traumatic brain injury (TBI) and controls in the performance-based assessments at 7-year follow-up.

	TBI					Controls					<i>t</i>	<i>p</i> [†]
	<i>n</i> = 27					<i>n</i> = 27						
	N	M	SD	Min	Max	N	M	SD	Min	Max		
Performance-based measures												
Wechsler scales												
Full Scale Intellectual Quotient	26	90.3	16.3	68	129	27	101.7	12.0	78	124	2.9	0.005
Working Memory Index	27	93.7	14	67	124	-	-	-	-	-		
Test of Attentional Performance	27					27						
<i>Divided Attention</i>												
Visual Attention - Mean RT (ms)		944.0	241.4	559	1502		848.0	177.2	559	1242	-1.7	0.102
Visual Attention - False alarms		2.4	4.2	0	19		0.7	1.0	0	4	-2.02	0.053
Visual Attention - Omissions		3.0	2.6	0	8		2.5	2.5	0	8	-0.7	0.489
Auditory Attention - Mean RT (ms)		614.8	88.8	434	773		588.2	103.5	425	795	-1.01	0.315
Auditory Attention - False alarms		1.4	2.0	0	7		0.4	1.0	0	4	-2.3	0.028
Auditory Attention - Omissions		0.6	0.8	0	3		0.1	0.3	0	1	-2.9	0.006

Dual Task - Auditory RT (ms)	667.2	200.3	405	1244	623.0	156.6	309	991	-0.9	0.370
Dual Task - Visual RT (ms)	901.3	231.4	620	1747	791.2	160.5	532	1195	-2.03	0.047
Dual Task - False alarms	3.2	4.4	0	14	0.6	1.6	0	8	-2.9	0.006
Dual Task - Auditory Omissions	1.9	2.6	0	9	0.9	1.7	0	6	-1.7	0.105
Dual Task - Visual Omissions	3.2	2.9	0	10	1.8	2.1	0	8	-2.01	0.049
Dual Task - Total Omissions	5.1	4.3	0	14	2.7	3.3	0	12	-2.3	0.024

Flexibility

Digits - Mean RT (ms)	607.0	139.1	418	959	540.1	154.5	322	967	-1.7	0.100
Digits - Errors	2.0	2.0	0	6	2.3	2.4	0	9	0.6	0.543
Letters - Mean RT (ms)	561.1	155.9	365	861	530.5	183.6	351	1133	-0.06	0.512
Letters - Errors	2.2	1.8	0	6	1.6	1.2	0	4	-1.4	0.162
Digits & Letters - Mean RT (ms)	891.7	276.4	477	1488	755.1	266.6	400	1249	-1.8	0.070
Digits & Letters - Errors	12.1	8.4	0	29	6.1	5.7	0	23	-3.1	0.004

Inhibition

Go-No Go - Mean RT (ms)	445.7	100.1	302	679	419.7	82.4	292	609	-1.04	0.302
Go-No Go - False alarms	3.0	2.8	0	8	1.9	2.7	0	10	-1.5	0.135

Go–No Go - Omissions	0.7	1.8	0	7	0.3	1.2	0	6	-0.9	0.328
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Total scores

Reaction time (ms)	704.1	137.6	498.4	1029.9	636.9	136.1	453.5	942.8	-1.8	0.077
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Errors	9.8	6.4	0.5	22.5	5.4	3.7	0.7	15.9	-3.1	0.003
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Errands test

Total number of errors	8	2.6	1.5	0	5	7	1.9	1.3	0	3	-1.03	0.319
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Six-part test

Standard score	18	8.4	1.9	4	12	19	8.7	3.0	4	15	0.35	0.731
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[†] Student *t*-test; M, mean; SD, standard deviation; Min, minimum; Max, maximum; RT, reaction time; ms, milliseconds.

Table 3. Comparison of participants with TBI and controls in the parent reports of the Behavior Rating Inventory of Executive Function (BRIEF) at 7-year follow-up.

	TBI					Controls					<i>t</i>	<i>p</i> [†]
	<i>n</i> = 27					<i>n</i> = 27						
	M	SD	Min	Max	≥ 65	M	SD	Min	Max	≥ 65		
BRIEF (Parent reports)												
Inhibit	56.9	16.8	33	90	26%	47.1	10.8	36	81	7%	-2.6	0.014
Shift	58.2	15.2	37	94	26%	48.7	10.4	36	73	7%	-2.7	0.010
Emotional control	61.3	16.9	37	97	37%	50.3	8.0	37	68	4%	-3.04	0.004
Initiate	54.1	12.2	34	77	26%	52.3	12.6	36	84	19%	-0.6	0.586
Working memory	62.6	14.3	40	98	44%	48.8	10.4	38	77	7%	-4.1	0.0002
Plan/Organize	56.2	12.7	37	81	26%	49.0	11.5	36	73	19%	-2.2	0.033
Organization of materials	54.1	11.4	35	79	15%	50.6	8.2	35	67	7%	-1.3	0.195
Monitor	55.6	12.0	34	85	22%	48.9	10.1	34	72	7%	-2.2	0.033
BRI	60.6	18.4	35	99	37%	48.8	8.5	37	69	4%	-3.03	0.005
MI	57.7	12.7	37	81	30%	49.8	11.5	37	72	15%	-2.4	0.020

GEC	59.5	15.2	37	89	44%	50.2	10.7	37	73	15%	-2.6	0.012
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[†] Student *t*-test; M, mean; SD, standard deviation; Min, minimum; Max, maximum; BRI, Behavioral Regulation Index; MI, Metacognition Index (MI); GEC, Global Executive Composite; ≥ 65 , percentage of participants of each group scoring beyond the clinical cut-off for the BRIEF.

Table 4. Comparison of participants with TBI and controls in the questionnaire-based assessments at 7-year follow-up.

	TBI					Controls					<i>t</i>	<i>p</i>
	<i>n</i> = 27					<i>n</i> = 27						
	N	M	SD	Min	Max	N	M	SD	Min	Max		
<i>Questionnaire-based measures</i>												
<i>Parent reports</i>												
Behavior (CBCL/ABCL)												
Internalizing problems	26	60.9	11.0	41	89	26	56.9	9.8	33	74	-1.4	0.166
Externalizing problems	26	55.8	11.6	33	73	26	48.8	6.8	34	66	-2.7	0.011
Total problems	26	58.9	10.6	39	76	26	50.3	9.1	25	69	-3.2	0.003
Health-related quality of life												
Total score (PedsQL)	19	72.7	18.2	34.8	96	20	83.0	17.0	47.8	100	1.8	0.076
Fatigue												
Total score (MFS)	19	67.2	21.7	31.9	100	20	87.6	11.4	58.3	100	3.7	0.001
Family functioning												
Total score (FAD)	26	1.7	0.4	1	2.7	27	1.6	0.4	1	2.6	-0.6	0.571

Self-reports

Behavior (YSR/ASR)

Internalizing problems	19	58.9	11.4	35	84	19	56.4	10.1	39	81	-0.72	0.474
Externalizing problems	19	56.7	11.1	37	75	19	50.2	5.9	41	59	-2.3	0.032
Total problems	19	57.4	11.1	35	75	19	51.7	8.0	37	67	-1.8	0.075

Health-related quality of life

Total score (PedsQL)	26	72.4	18.3	34.8	98.9	27	85.2	12.0	54.3	100	3	0.005
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Fatigue

Total score (MFS)	26	60.6	18.4	27.8	90.3	27	80.1	13.7	52.8	97.2	4.4	0.0001
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[†] Mantel-Haenszel chi-square test; CBCL/ABCL, Child/Adult Behavior Checklist; YSR/ASR, Youth/Adult Self Report; PedsQL, Pediatric Quality of Life inventory; MFS, Multidimensional Fatigue Scale; FAD, Family Assessment Device.

Table 5. Associations of the BRIEF (parent report) and the Test of Attentional Performance (TAP) scores with performance- and questionnaire-based assessments in participants with TBI at 7 years post-injury.

	BRIEF			TAP					
	GEC			Reaction Time			Errors		
	N	<i>r</i>	<i>p</i>	N	<i>r</i>	<i>p</i>	N	<i>r</i>	<i>p</i>
<i>Performance-based measures</i>									
Intellectual ability									
Full Scale Intellectual Quotient	26	-0.35	0.079	26	-0.48	0.015	26	-0.51	0.009
Working Memory Index	27	-0.24	0.236	26	-0.12	0.561	26	-0.20	0.348
<i>Questionnaire-based measures</i>									
<i>Parent-reports</i>									
Behavior (CBCL)									
Internalizing problems	26	0.60	0.0013	26	0.15	0.466	26	0.12	0.578
Externalizing problems	26	0.80	<0.0001	26	0.26	0.215	26	0.43	0.033
Total problems	26	0.87	<0.0001	26	0.31	0.138	26	0.40	0.049

Health-related quality of life

Total score (PedsQL)	19	-0.66	0.002	19	-0.43	0.074	19	- .62	0.006
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Fatigue

Total score (MFS)	19	-0.72	0.0005	19	-0.38	0.121	19	-0.31	0.205
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Family functioning

Total score (FAD)	26	0.49	0.012	26	-0.28	0.170	26	-0.08	0.718
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Self-reports

Behavior (YSR/ASR)

Internalizing problems	19	0.25	0.307	19	0.27	0.287	19	0.26	0.308
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Externalizing problems	19	0.53	0.021	19	0.44	0.071	19	0.50	0.035
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Total problems	19	0.45	0.054	19	0.37	0.128	19	0.36	0.138
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Health-related quality of life

Total score (PedsQL)	26	-0.23	0.260	26	-0.49	0.013	26	-0.14	0.498
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Fatigue

Total score (MFS)	26	-0.24	0.231	26	-0.31	0.129	26	-0.01	0.958
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CBCL, Child Behavior Checklist; YSR/ASR, Youth/Adult Self Report; PedsQL, Pediatric Quality of Life inventory; MFS, Multidimensional Fatigue Scale; FAD, Family Assessment Device.