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ORIGINAL ARTICLE

Early neuropsychological profile of children diagnosed with a brain tumor predicts later academic difficulties at school age

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Abstract

Purpose Children diagnosed with a brain tumor (BT) in the first years of their life are at high risk of cognitive and neuropsychological problems, more school difficulties, and an increased need for educational support. To improve this condition, it will be beneficial to be able to identify the neuropsychological variables that are early predictors of school competences at later ages.

Methods We longitudinally assessed 30 school-age BT children with a diagnosis before the age of 5 who were administered cognitive and neuropsychological evaluations before entering school or in the first 2 school years and who were followed up for academic performance at least one year after the first evaluation. A discriminant function analysis was conducted to detect the early neuropsychological profile that best predicted those children who turned out to need school support or not; we tested 5 block multiple regression models, one for each academic variable entering as predictors the neuropsychological variables that significantly discriminated the two groups.

Results A total of 93.3% of the cases were correctly classified according to the discriminant function in "with vs. without" educational support. Visual attention abilities were highly correlated with resulting school problems, both for reading (accuracy and speed) and math (operations) at school age.

Conclusions Analysis provided evidence that the early neuropsychological profile may predict academic difficulties for both reading and math at school age and that visual attention seems to play an important role in both these academic abilities, allowing clinicians to identify children with major difficulties in/from early years and to intervene beforehand.

Keywords School support · Visual attention · Reading · Math · Brain tumor

Introduction

Brain tumors (BTs) are the most common solid tumor in children, and when a diagnosis of BT and consequent medical care occur before the age of 5 years, the majority of children enter school after having already finished the treatments [1]. The preschool and first school years are critical periods for the acquisition of new cognitive abilities preparatory for reading, writing, arithmetic, and understanding complex texts [1, 2], but also for the sensitivity of the brain development processes to environmental agents [2, 3]. Accordingly, several studies have reported that a younger age at diagnosis and treatment is a high-risk factor for a worse cognitive and neuropsychological outcome [1, 4, 5], demonstrating the child's developmental state is influenced by the neurological sequelae related to the tumor, the chosen treatments, and the possible complications [1].

Patients who have been diagnosed with cancer "grow into deficit": initial intellectual difficulties associated with illness and treatments are followed by later decline in higher-order

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cognitive functions: (i.e., attention, executive functions, and processing speed) [6, 7] even many years after the end of the therapies [7].

Impairments in cognitive functions increase the risk for young BT patients to develop more school problems than their peers [1, 7], with an excessive amount of time spent on their homework, difficulties in learning, in completing their school career and carrying on with further education, and in acquiring independence [7].

Research on preschool children with cancer and investigations into the correlations between early cognitive functioning and the development of late effects on academic performance is lacking [1, 2].

The main aim of this study is to understand the extent to which cognitive and neuropsychological assessment in preschool age or in the first 2 years of primary school can predict the need for school support in patients with BT. Identifying the neuropsychological variables that are early predictors of school competences at later ages can help with tailoring specific neuropsychological interventions aimed at strengthening the points of weakness and minimizing the gap caused by the tumor and its treatments.

With this aim, we longitudinally assessed 30 school-age children with a diagnosis of BT before the age of 5 who were administered cognitive and neuropsychological evaluations before entering school or in the first 2 school years and who were followed up for academic performance at least one year after the first evaluation.

Methods

Participants

Data on children with BT were retrospectively collected from the medical records of a pediatric rehabilitation center in Italy, the Scientific Institute I.R.C.C.S. E. Medea (Bosisio Parini). They included information on the presence or not of school support (assigned after a functional assessment or reported by parents) on the basis of which we subsequently divided the subjects into two respective groups.

At each evaluation session, all parents signed written informed consent for the use of the neuropsychological data of their children in an aggregate form for research purposes. The study protocol was approved by the local research Ethics Committee (Research no.14486).

Participants were eligible for the research if they met the following: (a) they were diagnosed with a BT at the age of 5 years or earlier; (b) they had a cognitive and neuropsychological evaluation including the Wechsler scales after 2 years and six months of age and before entering primary school or in the first 2 school years; (c) they had a follow-up evaluation of academic abilities at least one year after the first assessment; (d) they completed the treatments before the second assessment; and (e) they did not have any previous cognitive or sensory impairment. See Fig. 1.

The selection of patients is shown in Fig. 2. From the whole group of children with BT diagnosed before 5 and evaluated twice, we excluded children that did not undergo school assessment, the ones that were assessed as being too young (e.g., at the age of 3 and then 5 years old) or too old (e.g., at the age of 13 and then 17 years old).

Measures

Children's cognitive, neuropsychological, and academic assessment is shown in Table 1.

Statistical methods

All the test results were expressed as z scores to allow direct comparison between tests.

First, we identified which demographic, clinical, cognitive, and academic variables differ between the two groups of children (with and without school support). Independent-sample t tests (two-tailed) were used to compare continuous variables between the two groups or Fisher's exact test (2 sided) for nominal dichotomous ones.

Second, a discriminant function analysis (DFA) was conducted using the neuropsychological variables (see Table 1, "Neuropsychological functioning"), as predictors to identify the preschool neuropsychological profile of children who later needed school support or did not. A DFA classifies unknown individuals and the probability of their classification into a certain group. This way we could compare the real information about school support with theoretical information obtained from the algorithm of the DFA and test the efficiency of neuropsychological variable categorization.

The third step involved entering variables that significantly differentiated the two groups in the discriminant analysis into 5 multiple regression models, one for each academic variable.

The significance threshold was set at $p < 0.05$ in all statistical tests. Effect sizes were expressed as Cohen's d.

Results

Phase 1

Demographic, clinical, cognitive, and academic variables of whole group and of children with vs. without school support are reported in Tables 2 and 3. The majority of patients were females (56.66%), and most of the frequent diagnosis is medulloblastoma (33.33%), and followed by ependymoma (30%), of which 20% were of low grade. A large proportion of tumors were infratentorial (63.33%).

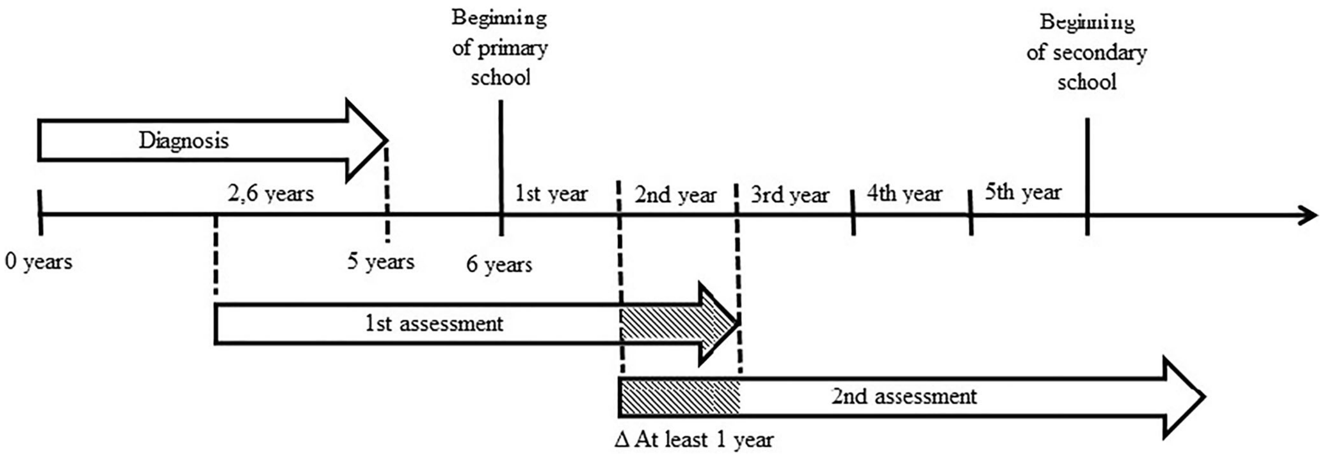

Fig. 1 Assessment timeline

Treatments undergone included both chemotherapy (83.33%) and radiotherapy (76.66%), with prevalence for focal treatment (43.33%). Hydrocephalus was present in 10 patients, with a consequent ventriculo-peritoneal shunt placement for all patients, but one was later converted into a ventriculo-atrial one.

Information about patient impairments after treatments was collected, as presence/absence. The most recurring one was

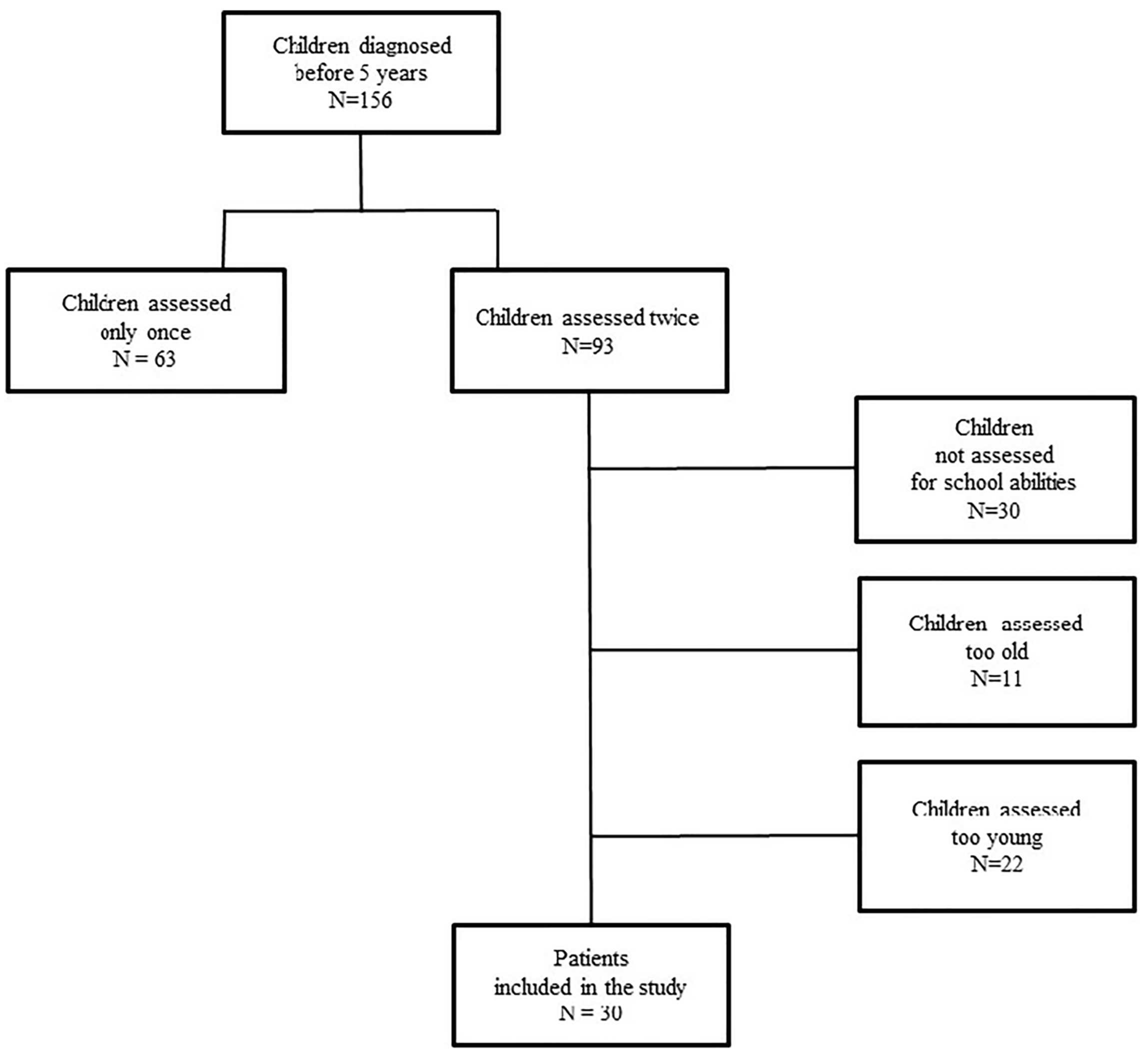

Fig. 2 Patient selection

Table 1 Cognitive and neuropsychological assessment

Domain	Test		Age	Measures
Cognitive functioning	Wechsler Preschool and Primary Scales of Intelligence, Revised (WPPSI-R) [8]		3–7.3 years	Verbal IQ
	Wechsler Preschool and Primary Scales of Intelligence Third Edition (WPPSI-III) [9]		2.6–7.3 years	Performance IQ
	Wechsler Intelligence Scale for children, Third Edition (WISC III) [10]		6–16.11 years	Full-scale IQ
Common subtests				
	Block design			Age scaled score
	Information			
	Vocabulary			
	Comprehension			
	Picture completion			
	Similarities			
Neuro-psychological functioning	Memory	Rey Complex Figure, Recall [11]	From 4 years	Correctness
		Corsi block-tapping test [12]	From 5 years	Correctness
		Selective Word Recall, immediate and delayed (BVN) [12]	From 5 years	Correctness
	Attention	Conners' Kiddie Continuous Performance Test [13]	4–7 years	Omissions
		Continuous Performance Test (CPT) [14]	From 8 years	
		Selective visual attention (from BVN) [12]	From 5 years	Correctness
	Executive function	Modified Card Sorting Test (MCST) [15]	4–13 years	Categories
		Wisconsin Card Sorting Test (WCST) [16]	6–70 years	
	Praxic abilities	Rey Complex Figure, Copy [11]	From 4 years	Correctness
	Visuo-spatial abilities	Rey Complex Figure, Copy [11]	From 4 years	Correctness
		Corsi block-tapping test (from BVN) [12]	From 5 years	Correctness
Academic functioning	Reading	MT-2 reading tasks for primary school [17]	6–11 years	Correctness
		New MT reading tasks for the 1st grade of secondary school [18]	11–14 years	Speed
		Evaluation of text comprehension: proposal of a deepening battery [19]	8–14 years	Correctness
	Mathematic	AC-MT 6–11 test. Test for evaluating calculation abilities [20]	6–11 years	Math operations
		AC-MT 11–14. Test for evaluating arithmetic and problem-solving abilities [21]	11–14 years	Time problems

IQ, intelligence quotient; BVN, neuropsychological evaluation battery for the developmental age

motor impairment (including hemiplegia or deambulation problems) followed by visual difficulties (such as nystagmus or double vision). Only a minority of the children developed auditory, language difficulties, or epilepsy. None of these sequelae were associated with the school support assignment ($p > 0.05$). See Table 2.

Mean age at radiotherapy was 44.38 months. Treatment lasted about 1 year for the majority of patients. Age at first (mean 66.588 months) and second assessments (117.530 months) had a comparable distribution in both samples.

The group without educational support showed significantly higher scores in Verbal Intelligence Quotient (IQ; 104.53 ± 11.38 vs. 88.69 ± 13.11; $t_{28} = 3.53$, $p = 0.001$), Performance IQ (103.65 ± 14.65 vs. 88.15 ± 12.15; $t_{28} = 3.08$, $p = 0.005$), and Full-Scale IQ (102.76 ± 11.91 vs. 85.85 ± 11.64; $t_{28} = 3.89$, $p = 0.001$). For age at diagnosis, age at 1st and 2nd evaluation, and delta between 2nd and 1st evaluation, we did not find any significant differences. Comparison of the academic performance measures revealed that the two groups significantly differed only in Reading Speed, with patients without school help showing significantly higher scores (− 0.299 ± 0.864) than children with educational support (− 1.652 ± 1.253; $t_{28} = 3.5$, $p = 0.002$). Non-significant differences were found for Reading Accuracy and Comprehension and Math Speed (all $p > 0.1$), but a trend for greater impairment in children who received school support at Math Operations was noted (− 1.2 ± 1.17 vs. − 0.37 ± 1.27; $t_{28} = 1.83$, $p = 0.078$) (see Table 3).

Phase 2

A DFA was conducted to detect the early neuropsychological profile that best predicted the need for school support. The best canonical discriminant function had an eigenvalue of 2.112 and a canonical correlation of 824 ($\chi^2 = 24.408$, df = 13, $p = 0.028$). A total of 93.3% of the cases were correctly classified according to this function, with no children who did not receive school support being classified as requiring it (i.e., false alarms), and 2 children who received school support being classified as not requiring school support (i.e., false negatives). Thus, the classification power of the discriminant analysis procedure was quite good, with nine predictors significantly differentiating them (see Table 4, significant p-values flagged as *).

Phase 3

To better delineate which specific aspects of academic performance were predicted by each early neuropsychological

Table 2 Demographic, clinical variables, and related Fisher exact-test comparisons

	Whole group ($N = 30$) N (%)	No educational support ($N = 17$)	Educational support ($N = 13$)	p value
Sex (males)	13 (43.33%)	8 (47.05%)	5 (38.46%)	0.721
Diagnosis				0.461
Medulloblastoma	10 (33.33%)	5 (29.41%)	5 (38.46%)	
Ependymoma	9 (30%)	4 (23.52%)	5 (38.46%)	
Glioma	8 (26.66%)	6 (35.29%)	2 (15.38%)	
Low grade	6 (20%)	5 (29.41%)	1 (7.69%)	
High grade	2 (6.66)	1 (11.76%)	1 (7.69%)	
Other	3 (10%)	2 (11.76%)	1 (7.69%)	
Carcinoma of the choroid plexuses	1 (3.33%)	1 (5.88%)	0 (0%)	
Meningioma	1 (3.33%)	0 (0%)	1 (7.69%)	
Teratoid rhabdoid tumor	1 (3.33%)	1 (5.88%)	0 (0%)	
Tumor location				0.708
Supratentorial	11 (36.66%)	7 (41.17%)	4 (30.76%)	
Infratentorial	19 (63.33%)	10 (58.82%)	9 (69.23%)	
Cerebellar vermis	5 (16.66%)	3 (17.64%)	2 (15.38%)	
Brain stem	3 (10%)	1 (5.88%)	2 (15.38%)	
Posterior cranial fossa	3 (10%)	2 (11.76%)	1 (7.69%)	
IV ventricle	7 (23.33%)	4 (23.52%)	3 (23.07%)	
Radiotherapy	23 (76.66%)	12 (70.58%)	11 (84.61%)	0.672
Type of radiotherapy				0.697
Craniospinal	10 (33.33)	6 (35.29%)	4 (30.76%)	
Focal	13 (43.33%)	6 (35.29%)	7 (53.84%)	
Hydrocephalus	10 (33.33%)	5 (29.41%)	5 (38.46%)	0.705
Visual impairment	9 (30%)	4 (23.52%)	5 (38.46%)	0.443
Auditory impairment	4 (13.33%)	1 (5.88%)	3 (23.07%)	0.290
Motor impairment	13 (43.33%)	5 (29.41%)	8 (61.53%)	0.138
Language impairment	6 (20%)	1 (5.88%)	5 (38.46%)	0.061
Epilepsy	3 (10%)	2 (11.76%)	1 (7.69%)	0.100

variable identified, we tested 5 block multiple regression models, one for each academic variable (i.e., Reading Accuracy, Speed and Comprehension, and Math Operations and Speed), entering as predictors the neuropsychological variables that significantly differentiated the two groups (Table 5). Only the immediate but not the delayed score of the Selective Word Recall subtest was entered to avoid collinearity. A preliminary check ensured the absence of collinearity between the remaining 8 predictors (all $-0.025 < r < 0.669$), ensuring that less than 45% of variance was shared by any two predictors.

The regression model with Reading Accuracy as dependent variable was significant (adjusted $R^2 = 0.292$; $F_{8,29} = 2.5$, $p = 0.044$), with Selective visual attention and M/WCST Category scores being the best predictors ($p < 0.01$); the Selective Word Recall score was also marginally significant as a predictor ($p = 0.038$), but it surprisingly showed a negative association with Reading Accuracy.

The regression model with Reading Speed as dependent variable was also significant (adjusted $R^2 = 0.35$; $F_{8,29} = 2.96$, $p = 0.022$), but only Selective visual attention was a significant predictor ($p = 0.021$). Conversely, the model did not reach significance for Reading Comprehension (adjusted $R^2 = 0.228$; $F_{8,29} = 2.07$, $p = 0.087$); and no predictors were significant, with the exception of a tendency for the M/WCST category score ($p = 0.069$).

Non-significant models were found for both Math Operations (adjusted $R^2 = 0.223$; $F_{8,128} = 2$, $p = 0.099$) and Speed (adjusted $R^2 = 0.082$; $F_{8,27} = 1.3$, $p = 0.3$). Nevertheless, Selective Visual Attention was a significant predictor of Math operation abilities ($p = 0.04$), while Wechsler Vocabulary significantly predicted Math Speed ($p = 0.033$).

Table 3 Descriptive statistics and related t test comparisons

	Whole group ($N = 30$) M (SD)	No educational support ($N = 17$)	Educational support ($N = 13$)	t	df	p value
Age at diagnosis (months)	39.40 (19.06)	40.70 (19.96)	40.07 (17.7786)	0.090	28	0.929
Age at radiotherapy (months) ($N = 24$)	44.38 (20.46)	40.25 (20.86)	46.18 (19.29)	− 0.395	22	0.697
Treatment duration (months)	11.57 (17.05)	12.12 (22.43)	10.85 (5.58)	0.225	28	0.825
Age at 1st assessment (months)	68.07 (12.09)	66.58 (10.94)	70.00 (13.65)	− 0.760	28	0.453
Age at 2nd assessment (months)	119.07 (25.88)	117.53 (24.59)	118.31 (21.46)	− 0.091	28	0.928
Time occurring between 1st and 2nd assessment (months)	51.00 (26.37)	50.94 (24.51)	48.30 (25.12)	0.288	28	0.775
Verbal IQ	97.67 (14.36)	104.53 (11.38)	88.69 (13.11)	3.536	28	0.001*
Performance IQ	96.93 (15.51)	103.65 (14.65)	88.15 (12.15)	3.083	28	0.005*
Full-scale IQ	95.43 (14.39)	102.76 (11.91)	85.85 (11.64)	3.890	28	0.001*
Reading accuracy	0.04 (0.66)	0.22 (0.53)	− 0.17 (0.77)	1.673	28	0.105
Reading speed	− 0.88 (1.23)	− 0.29 (0.86)	− 1.65 (1.25)	3.501	28	0.002*
Reading comprehension	− 0.30 (0.92)	− 0.09 (0.83)	− 0.57 (0.98)	1.453	28	0.157
Math operations	− 0.74 (1.27)	− 0.36 (1.27)	− 1.20 (1.16)	1.833	27	0.078
Math speed	− 0.57 (3.09)	− 0.37 (3.79)	− 0.84 (1.94)	0.393	26	0.698

IQ, intelligence quotient; M, mean; SD, standard deviation

*Significant p values at $p < 0.05$

Discussion

In the present study, we aimed to identify which neuropsychological dysfunctions at an early age were more indicative of the child's need to receive school support in a population of 30 BT survivors diagnosed before the age of 5. Of these patients, 13 received school support and 17 did not at the time of the study. Comparison of the clinical, neuropsychological, and academic profile of the two groups revealed that children who received educational support had lower IQ scores, both in verbal and non-verbal domains, which were in the borderline functioning range.

In Italy, the assignment of a support teacher is only allowed for children with a disability which is certified according to the International Classification of Functioning, Disability and Health, that does not consider the impairment, but the health,

Table 4 Means, standard deviations, and correlations with the discriminant function for every test

Neuropsychological variables	No educational support M (SD)	Educational support	p value	Function
Selective Word Recall, immediate	0.13 (0.94)	− 1.79 (1.95)	0.001*	0.464
Selective Word Recall, delayed	0.45 (0.81)	− 0.83 (1.21)	0.002*	0.451
Wechsler Information	10.88 (2.11)	8.00 (2.73)	0.003*	0.423
Wechsler Comprehension	10.11 (2.20)	7.46 (2.81)	0.007*	0.377
Rey Complex Figure, Copy condition	− 0.37 (0.84)	− 1.77 (1.94)	0.012*	0.348
Wechsler Block Design	10.88 (3.29)	8.23 (2.00)	0.016*	0.332
M/WCST Category	0.53 (1.24)	− 0.53 (1.09)	0.019*	0.323
Wechsler Vocabulary	10.58 (2.47)	8.84 (1.62)	0.037*	0.286
Selective visual attention	0.001 (0.77)	− 0.70 (1.08)	0.045*	0.272
Wechsler Picture Completion	10.17 (2.24)	8.61 (3.06)	0.118	0.210
K/CPT Omissions	− 0.42 (1.29)	0.14 (0.72)	0.163	− 0.186
Rey Complex Figure, Memory condition	− 1.05 (1.04)	− 1.25 (1.36)	0.657	0.058
BVN Corsi block-tapping test	− 0.17 (1.01)	− 0.30 (0.92)	0.715	0.048

M, mean; SD, standard deviation

*Significant p values at $p < 0.05$

Table 5 Results of multiple regression analysis on neuropsychological variables predicting academic competence

	Reading Accuracy		
	ß	*t*	*p* value
Wechsler Block Design	− 0.199	− 1.041	0.310
Wechsler Information	− 0.449	− 1.612	0.122
Wechsler Vocabulary	0.448	1.863	0.077
Wechsler Comprehension	0.085	0.415	0.682
M/WCST Category	0.594	2.844	0.010*
Rey Complex Figure, Copy condition	0.041	0.187	0.853
Selective visual attention	0.624	3.310	0.003*
Selective Word Recall, immediate	− 0.511	− 2.213	0.038*
	Reading speed		
	ß	*t*	*p* value
Wechsler Block Design	− 0.274	− 1.494	0.150
Wechsler Information	0.428	1.601	0.124
Wechsler Vocabulary	− 0.073	− 0.319	0.753
Wechsler Comprehension	0.254	1.286	0.213
M/WCST Category	− 0.027	− 1.137	0.892
Rey Complex Figure, Copy condition	0.287	1.371	0.185
Selective visual attention	0.451	2.499	0.021*
Selective Word Recall, immediate	− 0.119	− 0.539	0.596
	Reading comprehension		
	ß	*t*	*p* value
Wechsler Block Design	0.111	0.555	0.584
Wechsler Information	− 0.030	− 0.104	0.918
Wechsler Vocabulary	0.185	0.738	0.469
Wechsler Comprehension	− 0.036	− 0.168	0.868
M/WCST Category	0.418	1.914	0.069
Rey Complex Figure, Copy condition	0.203	0.889	0.384
Selective visual attention	0.108	0.549	0.589
Selective Word Recall, immediate	0.056	0.230	0.820
	Math operation		
	ß	*t*	*p* value
Wechsler Block Design	0.108	0.509	0.616
Wechsler Information	0.033	0.112	0.912
Wechsler Vocabulary	0.245	0.954	0.352
Wechsler Comprehension	− 0.095	− 0.426	0.675
M/WCST Category	0.274	1.228	0.234
Rey Complex Figure, Copy condition	0.003	0.012	0.991
Selective visual attention	0.441	2.197	0.040*
Selective Word Recall, immediate	0.051	0.208	0.837
	Math speed		
	ß	*t*	*p* value
Wechsler Block Design	0.040	0.169	0.867
Wechsler Information	− 0.394	− 1.112	0.280
Wechsler Vocabulary	0.752	2.302	0.033*
Wechsler Comprehension	0.440	1.637	0.118
M/WCST Category	− 0.144	− 0.628	0.537
Rey Complex Figure, Copy condition	− 0.466	− 1.774	0.092
Selective visual attention	0.280	1.247	0.228
Selective Word Recall, immediate	− 0.109	− 0.418	0.681

*Significant *p* values at $p < 0.05$

potential, and resources of the individual. Since the school demand is based on the student needs, it follows that IQ is a very important factor.

Interestingly, comparing the academic performance of children with vs. without school support, the children only differed in reading speed and, marginally, in the ability to complete math operations.

Reading speed increases from elementary school until young adulthood and, beyond linguistic skills, is heavily predicted by visual information processing speed, since fluent reading requires simultaneously processing different letters in a very short time to identify a word [22]. The development of information processing speed partially depends on the integrity of white matter, which is particularly vulnerable to radiotherapy [5]. Processing speed decline is a typical sign of posterior fossa tumors [4]. Since the majority of our patients had an infratentorial tumor, which frequently received craniospinal irradiation, it is not surprising that reading speed difficulty was a major feature of patients who were deemed as requiring school support. This is also in keeping with recent evidence suggesting reduced processing speed was more related to reading disorders, while impairments in temporal processing and visuospatial memory were more associated with math disorders [23]. Nevertheless, both difficulties seem to share an important deficit in working memory [24]. Accordingly, we found a trend towards greater difficulties in math operations in school support groups.

To clarify which neuropsychological variables predicted academic difficulties, we tested a DFA to predict, on the basis of the early neuropsychological profile, which patients would need educational support. The results showed that the early neuropsychological profile of children was a good predictor of special education needs at school age, because 93.3% of original grouped cases were correctly classified, providing a reliable cue about who will probably have major difficulties. From a psycho-pedagogical perspective, it is important to study survivors' performances following diagnosis and treatments, in order to better understand the needs of these children and to intervene earlier on the relevant cognitive prerequisites, in order to minimize learning difficulties at school.

To identify the cognitive prerequisites for successful academic learning, we tested with standard regression models which neuropsychological variables were more likely to predict specific academic difficulties. The models were significant for both Reading Accuracy and Reading Speed, suggesting that the early neuropsychological evaluation provided a good indication of reading difficulties at school. Importantly, selective visual attention was a good predictor of both Reading Accuracy and Speed, while executive functions, as measured by the M/WCST Category, predicted Reading Accuracy but not Reading Speed.

Attention mechanisms have a close relationship with phonological awareness and word and pseudo-word reading [25]. Selective spatial attention is essential for accurately reading words. Visual attention capacity could limit reading speed in primary school children [22] because it could be affected by poor visual-search abilities [26, 27].

The number of categories completed in the M/WCST is a strong predictor of reading accuracy; indeed reading words and pseudo-words is linked to self-regulation (and executive functions) [25], which prevents guessing or anticipating the word the child is reading. Accordingly, Helland and Asbjørnsen [28] found fewer WCST categories completed in children with dyslexia as compared with age-matched controls [28].

When word decoding becomes an automatic process, text comprehension is mainly supported by working memory and metacognitive skills, allowing the reader to perform higher-level tasks [29]. No variables in our sample were associated with Reading Comprehension, probably because the level of literacy reached by our patients was not strong enough to differentiate higher-level reading skills.

Surprisingly, no significant prediction power was offered by preschool verbal abilities. We only observed a trend towards significance for vocabulary abilities to predict Reading Accuracy. Decoding new words in healthy children needs good vocabulary skills, which could help them to better understand words they have never met before, using the surrounding text. A good vocabulary knowledge is necessary not only for word identification [30], but it is also a good predictor of reading comprehension [31]. Nevertheless, preschool vocabulary knowledge was not able to predict reading accuracy, speed or comprehension at school age in our sample.

We found only weak predictors for mathematical skills. Both verbal [32] and non-verbal, such as visuospatial attention [33], cognitive functions are involved in mathematical development. These functions may be affected by tumor and treatments, thus leading to difficulties in mathematics learning. Unfortunately, our assessment lacked evaluation of verbal components, such as verbal working memory and phonological processing; however, we detected an association between vocabulary skills and Math Speed and between visual attention and Math Operations.

It is well known that language-based abilities and vocabulary are significantly associated with math skills in typically developing children [34]. Expressive vocabulary is crucial for understanding and learning through classroom teaching, especially in verbal problem solving [35]. Moreover, numerical competence is a precursor of math abilities [36] and can be represented in two ways in children: using the approximate number system, which is not dependent on language, or using the exact number system, which, is slowly developed as children learn number words [37].

A pattern of impairment with regard to reading and attention has been recognized in our patients that can be found also in children with Specific Learning Disabilities: for example dyslexic children have a deficit in orienting and focusing attention [26] or children with Attention Deficit Hyperactivity Disorder have lower academic achievement than peers [38]. These results suggest that even if cognitive core deficits underlying these disorders are different, domain-general risk factors might be in common [23].

Finally, we explored why some tests did not show any significant correlations with the discriminant functions: Wechsler Figure Completion and CPT Omissions are both related to the ability to distinguish between essential and non-essential details, necessary in learning, and connected with sustained attention and executive functions. The Rey Figure and Corsi tapping tests are both linked to the visuospatial working memory. Therefore, the lack of correlations between these tests with the discriminant function might be related to the fact that these measures are more supported by executive functions that develop throughout the life cycle [25].

Limitations of this study should be acknowledged. First, because of the inclusion criteria we have chosen, it is possible that some bias in the selection of the patients could be present. It turns out that our sample is relatively small (only 22% of the children diagnosed before 5 satisfied the selection criteria) and, consequently, generalization to the global population of children with a brain tumor diagnosed before 5 years of age is limited. Second, the clinical variables of our patients are very different in terms of diagnosis, tumor locations and treatments. A larger sample is needed to better investigate important features and processes that can occur in preschool years. Furthermore, having more homogenous samples may allow investigations into whether diagnosis, tumor location, specific treatments or other clinical variables could differently impact school development trajectories. Finally, it would be useful to broaden the spectrum of neuropsychological variables considered, including, in particular, working memory and decoding abilities.

To our knowledge, this is the first attempt to investigate long-term school abilities from an early neuropsychological assessment in children with a diagnosis of BT before the age of 5. Analysis provided evidence that the early neuropsychological profile may predict academic difficulties for both Reading and Math at school age and that visual attention seems to play an important role in both these academic abilities. This finding may allow clinicians to identify children with major difficulties in/from their early years, intervening beforehand to minimize as much as possible the gap between survivors and their healthy peers.

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Data availability The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

Compliance with ethical standards

Conflict of interest/competing interests The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in this study were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study protocol was approved by the local research Ethics Committee (Research n.14486).

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