Acta Neurochirurgica (2019) 161:161–169
https://doi.org/10.1007/s00701-018-3744-0

ORIGINAL ARTICLE - PEDIATRIC NEUROSURGERY

Mathematical skills in children with pilocytic astrocytoma

Silvia Benavides-Varela[1,2,3] · Riccardina Lorusso[4,5] · Valentina Baro[4] · Luca Denaro[4] · Nancy Estévez-Pérez[6] · Daniela Lucangeli[1] · Domenico D'Avella[4] · Carlo Semenza[3,4]

Received: 30 July 2018 / Accepted: 20 November 2018 / Published online: 6 December 2018

Abstract

Background Pediatric patients with circumscribed cerebellar pilocytic astrocytoma (PA) tumors generally perform within the normal range on neuropsychological tests after a complete tumor resection. The outcome in academically relevant abilities such as mathematics, which in adults involve some cerebellar functions, is however much less understood. The aim of this study is to retrospectively investigate the neuroplasticity of mathematical skills and associated cognitive functions following cerebellar resection of PA in pediatric patients.

Methods Twenty-two children (mean age = 11.2 $\pm$ 1.8), including 11 PA patients (females = 6) and 11 healthy controls (females = 6), were administered a battery of mathematical (MaT) and neuropsychological tests. Single-case statistical analyses were carried out (Crawford's t) as well as between-group comparisons (Wilcoxon test). Spearman correlations between MaT and neuropsychological tests were calculated.

Results Thirty-six percent of the patients showed difficulties in some mathematical tasks, 50% of them within a broader cognitive deficit. Verbal working memory was associated with MaT performance both in patients and controls while, crucially, visuospatial memory, and visual-motor integration were associated with MaT in patients only. Among patients, MaT correlated negatively with tumor size and positively with the interval surgery test.

Conclusions The results evince an overall recovery of mathematical abilities despite PA in the majority of patients. This functional reestablishment is supported by visuospatial and visuomotor integration functions that contribute to set up emerging mathematical skills in these patients. Higher levels of compensation are found in more developed tumors as compared to smaller ones.

Keywords Low-grade pilocytic astrocytoma · Surgical resection · Cerebellum · Neuropsychological sequelae · Mathematical performance

Introduction

Astrocytoma is the most common brain tumor diagnosed in childhood with an incidence of 35 per million in children below 15 years of age [21]. The most common variant in children is the pilocytic astrocytoma (PA). This tumor occurs anywhere in the central nervous system, but it is most frequently found in the cerebellum, in the optic pathways, and in the hypothalamus.

Silvia Benavides-Varela and R. Lorusso contributed equally to this work.

This article is part of the Topical Collection on *Pediatric Neurosurgery*

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s00701-018-3744-0) contains supplementary material, which is available to authorized users.

✉ Silvia Benavides-Varela
silviabenavides@gmail.com

1 Department of Developmental Psychology and Socialization, University of Padova, Via Venezia 8, 35131 Padova, Italy

2 Department of General Psychology, University of Padova, Via Venezia 8, 35131 Padova, Italy

3 IRCCS San Camillo Hospital Foundation, Neuropsychology Unit, Lido, Venice, Italy

4 Department of Neuroscience (Padova Neuroscience Center), University of Padova, Padova, Italy

5 Department of Medicine, University of Padova, Padova, Italy

6 Brain Development Laboratory, Cuban Neurosciences Centre, Havana, Cuba

Standard clinical interventions on patients diagnosed with PA entail surgical resection. Adjuvant therapies such as radiation and chemotherapy are rarely needed, and generally, the 10-year survival is over 90% [15]. This relatively high survival of patients diagnosed with PA calls for increasing efforts to evaluate short- and long-term neuropsychological outcomes and the path of cognitive development and scholastic attainment in these children.

Patients with circumscribed cerebellar tumors perform within the normal range of neuropsychological test norms. In particular, no significant differences between mean IQ measures in cerebellar and normal control groups have been reported [28]. However, a more detailed neuropsychological testing has revealed several problems in cognitive domains including attention, memory, visuo-constructive skills, language, processing speed, and interference [2, 16, 17, 20, 28]. Furthermore, significant impairments in visuospatial skills are seen in about 22% of cerebellar PA patients at a mean of 3 years post-treatment [1].

In spite of the fact that PA patients occasionally show cognitive deficits, the majority of these children attends the normal school programs and eventually incorporates in regular professional work [11]. From a neuropsychological point of view, these patterns may arise because functions besides those normally supporting the performance in more abstract tasks take over and compensate during ecological tasks [5, 6, 8]. At present, however, this is a hypothetical explanation as no previous study attempted to evaluate compensatory mechanisms and the relation with academic skills in this specific group of patients.

The current study attempted to fill in this gap by assessing a group of cerebellar PA patients and a control group of healthy children on various mathematical and neuropsychological tests. The correlation of some cognitive functions and mathematical tests was investigated separately for patients and controls as a means to shed some light on the way brain plasticity could lead to functional reestablishment of cognitive skills in development and following tumor resection in children. The hypothesis was that, if compensatory mechanisms take place after surgical resection, then different cognitive factors should link to the scholastic performance in PA patients and healthy children of the same age.

Particularly relevant for the present study are PA patients with circumscribed cerebellar tumors. The cerebellum is known historically for its involvement in motor functions and, in adults, it has been more recently implicated also in a wide range of high cognitive functions including number and calculation tasks [3]. The cognitive role of the cerebellum during development, however, is much less understood. Thus, although mathematical deficits in patients following cerebellar resection might be hypothesized based on the adult literature, the neurocognitive outcome might differ in pediatric populations.

Method

Participants

A group of 11 children (mean age = 11.2 $\pm$ 1.8; age range = 6.2–12.5; *N* females = 6; mean years of education 5.5; range 1–7) that underwent surgical resection for PA at the Academic Neurosurgery, University of Padova Medical School between 2006 and 2017 were included in this study. Diagnostic criteria of low-grade astrocytoma were determined by means of magnetic resonance imaging, and surgical intervention took place 0–2 days after diagnosis. Cerebellar astrocytoma was present in all the patients. Participants were excluded if any of the following criteria were met: (1) abnormal vision or hearing that could not be corrected to normal, (2) presence of a genetic or other neurological condition that could affect test performance, (3) presence of behavioral disorders. Additionally, a control group of 11 children matched with the patients' group by gender (*N* females = 6), age (mean age = 11.2 $\pm$ 1.8; age range = 7.1–12.8), and education (mean years of education 5.6; range 1–7) was also included in the study. There were no significant differences between the group of patients and the control group in age $\chi2(1) = .01$; $p = .92$, and scholastic attainment estimated in years of education $\chi2(1) = .38$; $p = .54$. Written informed consent was obtained from all parents' participants according to the Declaration of Helsinki. The institution's research ethics committee did not consider that their approval was needed for this study because it was a retrospective work concerning a neuropsychological follow-up routinely performed at our institution.

Mathematical tests and neuropsychological assessment

The basic numerical battery (BNB) [24] was used to examine numerical abilities of the participants. BNB is an item-timed computerized battery that includes the following tests:

Dot-enumeration test: randomly arranged dots ranging from 1 to 9 were presented on the computer display. Children were asked to enumerate the quantities and to respond as quickly as they could without making mistakes. Reaction times and errors were recorded by pressing the key corresponding to the number of dots enumerated. Eighteen trials were presented altogether, with each number from 1 to 9 being presented twice in a pseudorandom order.

Numerical magnitude comparison: children were presented with two digits (ranging from 1 to 9) on the computer display, one to the left and one to the right of the screen, and they were asked to compare the magnitude of numbers. Thirty-six trials were presented in a pseudorandom order. Five practice trials were given before starting the test. Reaction times and errors were recorded.

Mental arithmetic: 15 simple additions, 15 subtractions, and 15 multiplications were presented in three separate blocks. Items were presented on the computer screen in the form "2 + 4." Two practices trials were given before the start of each block. Children were asked to type in the answer as quickly as they could without making any mistakes. Reaction time (RT) was measured with the first keystroke. Errors were also recorded. First and second graders did not receive the multiplication block, because at the time of the assessment, they were starting to learn the multiplication tables.

Simple reaction time: children were asked to press the space bar as soon as they saw a square in the center of display. Twenty trials were presented. Five practice trials were given before starting the test. Reaction times were recorded with millisecond precision. Because it is considered a baseline measure of processing speed, this measure was not analyzed by itself. It was used instead to adjust the previously described tests by subtracting simple reaction time from the reaction time on each the tests.

Children with low numeracy tend to adopt strategies that produce generally accurate answers but extremely long response time latencies, or they would simply guess quickly, leading to inaccurate answers but short response time latencies. Thus, as in previous studies [24], efficiency measures of the BNB were used for statistical analyses because they take into account these factors better than accuracy measures alone. Note that higher scores represent worse performance (i.e., longer time taken to provide accurate responses) whereas lower scores indicate fast and accurate responses.

A battery of neuropsychological tests was also administered in order to evaluate specific cognitive impairments among patients. Furthermore, some of the neuropsychological tests were used to explore the cognitive correlates of mathematical performance in both groups of participants. The *WISC-IV* [30] provided a measure of general intellectual functioning and four composite scores by domain: Verbal Comprehension Index, Perceptual Reasoning Index, Working Memory Index, and Processing Speed Index. Furthermore, measures of *visual selective attention* were obtained from the cancelation subtest of the WISC-IV; *verbal short-term memory and working memory* were assessed using digit span forward and digit span backwards respectively. *Visuospatial short-term and working memory* were evaluated using the Corsi Block-Tapping test forwards and backwards respectively [19]. *Visual perceptual skills* were assessed using the Development Test of Visual-Motor Integration (VMI) and the two Supplemental Test: Visual-Spatial Perception (which does not require motor action) and Fine-Motor Accuracy Test [23].

Additional tests were administered to patients only. They included measures of *executive functions*: trial-making test (TMT-A, TMT-B, TMT-AB) [25] phonemic and semantic fluency [7] and *visuospatial memory and apraxia* (Rey–Osterrieth complex figure test) [18].

Statistical analysis

The comparisons of the patients and healthy control participants on the different neuropsychological and numerical tests were carried out using group and single-case analyses. Group comparisons were performed using non-parametric Wilcoxon rank sum test due to the lack of homogeneity of variance among the groups in numerous tests (Bartlett multiple-sample test for Total IQ, Working Memory Index, Dot-enumeration, numerical magnitude comparison, additions, subtractions; all $ps < 0.01$). Additionally, single-case's scores were compared to the scores obtained in the control sample using Crawford's t tests [10].

Furthermore, in order to determine the role of cognitive abilities underlying the performance on the numerical tasks, separate correlation analyses for patients and controls were carried out. Non-parametric Spearman correlation was assessed between the efficiency measures of the BNB and measures of verbal and visual working memory, attention, and VMI battery. The time between surgery and assessment (in days) and the tumor size (derived from the T1 contrast medium from the MRI and calculated on the two longest intersected diameters of the tumor according to the neuroradiological report) were also included in the correlation analyses performed on the group of patients.

Results

Table 1 shows the scores of the patients and controls (means and standard deviations), the p values from the group analyses, and the number of patients performing below cut-off according to the normative data in each test. Results at the group level showed no significant differences between patients and controls in any of the neuropsychological or mathematical tests. Figure 1 shows the results of both groups on the numerical tests of the BNB battery.

Single-case analyses indicated abnormal scorings in some of the patients (see Table 2 for a summary, and the Appendix for detailed results of the Crawford's test). Specifically, significant deficits in mathematics were observed in four patients; of those, two showed generalized neuropsychological and mathematical deficits and two manifested mathematical-specific difficulties. Fully spared neurobehavioral and numerical abilities were observed in 54% of the patients (6 out of 11). One participant showed a generalized cognitive deficit but spared numerical abilities.

Table 1 General scores of the patients and controls on the neuropsychological and mathematical assessments

Neuropsychological test	Cognitive domain	Patients' scores (mean + SD)	No. of patients below cut-off (normative data)	Controls' scores (mean + SD)	p value (Wilcoxon test)
WISC-IV	Verbal Comprehension Index	27.9 + 5.8		30.9 + 5.3	0.25
	Perceptual Reasoning Index	29.3 ± 10.3	1	30.5 ± 5.7	0.92
	Processing Speed Index	15.8 ± 6.4	1	18.4 ± 4.1	0.32
	Working Memory Index	17.5 ± 4.6		18.0 ± 2.2	0.62
	Intelligence quotient (IQ)	90.4 ± 23.3	1	97.8 ± 8.5	0.96
Corsi forward	Visuospatial short-term memory	4.8 ± 1.1		4.9 ± 1.0	0.87
Corsi backwards	Visuospatial working memory	4.0 ± 1.2	1	4.2 ± 0.8	0.79
WISC-IV Verbal Span (forward)	Verbal short-term memory	5.3 ± 1.0	1	5.4 ± 0.7	0.50
WISC-IV Verbal Span (backwards)	Verbal working memory	4.0 ± 1.1		3.5 ± 0.7	0.16
WISC-IV Cancelation	Visual selective attention	57.2 ± 18.0	2	62.8 ± 19.3	0.59
VMI	Visual-spatial perception	21.5 ± 3.4		21.6 ± 2.8	0.98
	Fine-motor accuracy	22.1 ± 4.6		23.9 ± 2.4	0.36
	Visual-motor integration	21.8 ± 4.2		23.3 ± 3.0	0.43
BNB					
Dot-enumeration (accuracy)	Counting abilities	94.2 ± 7.6%		97.2 ± 2.5%	0.38
Dot-enumeration (efficiency)	Counting abilities	1996.8 ± 759.7 ms		1876.6 ± 649.5 ms	0.99
Numerical magnitude comparison (accuracy)	Number comprehension	86.4 ± 18.5%		93.0 ± 7.4%	0.72
Numerical magnitude comparison (efficiency)	Number comprehension	1393.1 ± 987.3 ms		990.2 ± 829.6 ms	0.05
Additions (accuracy)	Arithmetic	91.8 ± 9.3%		90.3 ± 8.0%	0.47
Additions (efficiency)	Arithmetic	4169.9 ± 4762.9 ms		2647.2 ± 815.5 ms	0.81
Subtractions (accuracy)	Arithmetic	95.8 ± 5.0%		96.8 ± 3.5%	0.84
Subtractions (efficiency)	Arithmetic	3541.1 ± 3710.9 ms		2131.8 ± 923.1 ms	0.34
Multiplications (accuracy)	Arithmetic	89.3 ± 11.0%		86.8 ± 6.9%	0.20
Multiplications (efficiency)	Arithmetic	2711.0 ± 1229.0 ms		2896.2 ± 964.6 ms	0.56

Correlational results in control participants

The significant results of the correlation analyses are summarized in Table 3. Measures of verbal working memory correlated with the controls' performance on dot-enumeration ($r = -.67$; $p = .01$), numerical magnitude comparison ($r = -.67$; $p = .01$), and additions ($r = -.61$; $p = .03$). The correlations are negative, thus suggesting that the less the time

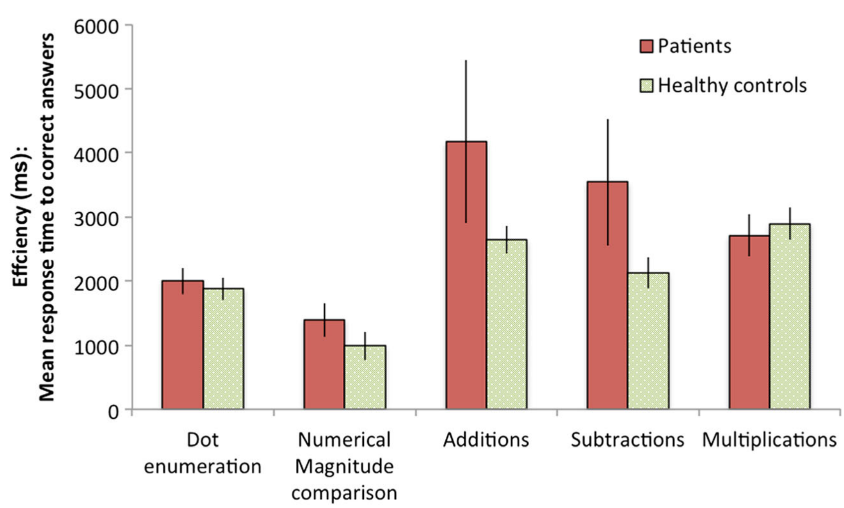

Fig. 1 Efficiency measures on the numerical tests of the BNB battery in both patients and control participants. Error bars depict standard errors of the mean

Table 2 Demographic, neurological, and neuropsychological outcome of the PA patients. Neuropsychological and mathematical outcomes are based on single-case Crawford's analyses

				Neurological assessment		
	Gender	Age (years)	Interval surgery-test (years)	Symptoms	Type of tumor	Associated hydrocephalus
Patient 1	F	12,4	2,9	Headache, ataxia, dizziness	Solid with a cystic	Yes
Patient 2	M	10,6	1,6	Headache, vomiting, papilledema, ataxia, oral production impairement	Solid with cystic components	Yes
Patient 3	F	12,2	1,4	Headache, vomiting, papilledema, ataxia, dizziness	Cystic with mural nodule	Yes
Patient 4	M	11,8	5,4	Headache, dizziness	Cystic with mural nodule	Yes
Patient 5	F	11,2	5,5	Headache, left eye, convergent strabism, vomiting	Solid	Yes
Patient 6	M	6,2	1,4	Right-sided occipital bone bulging	Cystic	No
Patient 7	M	10,0	2,7	Diplopia	Cystic	Yes
Patient 8	F	12,5	4,0	Headache, ataxia, dizziness, vomiting	Cystic	Yes
Patient 9	F	11,4	1,3	Headache, vomiting, papilledema, cervical pain	Cystic with mural nodule	Yes
Patient 10	F	10,6	1,0	Headache, vomiting, ataxia, dizziness	Solid	Yes
Patient 11	M	11,3	0,6	Headache, vomiting, ataxia, dizziness, blurred vision, writing impairment	Cystic with mural nodule	No

	Neurological assessment					Neuropsychological assessment
	Peri-operative complications	Hospitalization time (days)	Need for Rehabilitation	Size of the tumor	Surgical outcome	Neuropsychological deficits
Patient 1	None	11	None	62 × 72 mm	Excellent, no recurrence, no deficit	None
Patient 2	Mutism	24	Logopedic	60 × 45 mm	Excellent, no recurrence, no deficit	None
Patient 3	None	6	none	60 × 50 mm	Excellent, no recurrence, no deficit	None
Patient 4	None	12	none	60 × 50 mm	No recurrence, transient dysphagia	Perceptual Reasoning Index-WISC-IV**
Patient 5	None	20	none	38 × 39 mm	No recurrence-chemioTP	None
Patient 6	None	9	none	50 × 20 mm	Excellent, no recurrence, no deficit	Visuospatial working memory *; Visuospatial perception*; Fine-motor accuracy**
Patient 7	None	13	none	45 × 36 mm	excellent, no recurrence, no deficit	None
Patient 8	Left temporal extradural hematoma	23	none	53 × 62 mm	excellent, no recurrence, no deficit	None
Patient 9	None	9	none	48 × 54 mm	excellent, no recurrence, no deficit	None
Patient 10	None	55	motor and logopedic	52 × 67 mm	left hemiparesis, dysphagia, dysphonia, left hemisphere ischemia. No recurrence	None
Patient 11	CSF leak	35	motor and logopedic	42 × 46 mm	dysphagia, ataxia, conjugated eye movements impairement, diplopia	WISC-IV: Verbal Comprehension Index*, Working Memory Index*, Processing Speed Index**; Visuomotor integration*; Fine-motor accuracy**

*$p < .05$; **$p < .01$; ***$p < .005$

Table 3 Significant correlations between efficiency measures of the BNB numerical battery and neuropsychological tests in patients and controls

Controls					
Numerical tests BNB	Verbal working memory	Visual working memory	Visuomotor integration		
Dot-enumeration	$r = -.67; p = .01$*	$r = -.20; p = .51$	$r = -.59; p = .05$		
Numerical magnitude comparison	$r = -.67; p = .01$*	$r = -.39; p = .18$	$r = -.56; p = .06$		
Additions	$r = -.61; p = .03$*	$r = -.31; p = .32$	$r = -.33; p = .29$		
Subtractions	$r = -.56; p = .06$	$r = -.22; p = .50$	$r = -.40; p = .20$		
Multiplications	$r = -.02; p = .94$	$r = .44; p = .15$	$r = -.27; p = .40$		
Patients					
Numerical tests BNB	Verbal working memory	Visual working memory	Visuomotor integration	Tumor size	Time since surgery
Dot-enumeration	$r = -.88; p < .0001$***	$r = -.63; p = .02$*	$r = -.51; p = .07$	$r = -.65$; p = .02*	$r = -.45; p = .12$
Numerical magnitude comparison	$r = -.43; p = .13$	$r = -.68; p = .01$*	$r = -.58; p = .03$*	$r = -.63; p = .02$*	$r = -.05; p = .87$
Additions	$r = -.75; p = .003$***	$r = -.62; p = .02$*	$r = -.74; p = .004$***	$r = -.62; p = .02$*	$r = -.72; p = .007$*
Subtractions	$r = -.75; p = .003$***	$r = -.73; p = .005$**	$r = -.71; p = .006$**	$r = -.63; p = .02$*	$r = -.43; p = .14$
Multiplications	$r = -.50; p = .11$	$r = -.05; p = .89$	$r = -.32; p = .33$	$r = -.11; p = .75$	$r = -.65; p = .03$*

*$p < .05$; **$p < .01$; ***$p < .005$

taken for correctly answering in a given mathematical test (i.e., more efficient answers), the higher the scores in the neuropsychological tests.

Correlational results in cerebellar patients

Like in the control group, verbal working memory correlated with the performance on dot-enumeration ($r = -.88$; $p < .0001$), additions ($r = -.75$; $p = .003$), and subtractions ($r = -.75$; $p = .003$). In this group, and different from controls, also visual working memory correlated with various numerical tasks including dot-enumeration ($r = -.63$; $p = .02$), numerical magnitude comparison ($r = -.68$; $p = .01$), additions ($r = -.62$; $p = .02$), and subtractions ($r = -.73$; $p = .005$). Moreover, measures of visuomotor integration correlated with the patients' performance on numerical magnitude comparison ($r = -.58$; $p = .03$), additions ($r = -.74$; $p = .004$), and subtractions ($r = -.71$; $p = .006$).

A negative correlation was also found between the size of the tumor and the patients' efficiency on almost all the numerical tests: Dot-enumeration ($r = -.65$; $p = .02$), numerical magnitude comparison ($r = -.63$; $p = .02$), additions ($r = -.62$; $p = .02$), and subtractions ($r = -.63$; $p = .02$), indicating that the bigger the tumor, the less the time taken for correctly answering in a given mathematical test. Furthermore, the time surgery-test was negatively correlated with the patients' performance on additions ($r = -.65$; $p = .03$) and multiplications ($r = -.65$; $p = .03$), that is, the longer the time since the date of the surgical resection, the more efficient were the patients' responses to the mathematical test. None of the other neuropsychological tests correlated with the tests of the numerical battery. A summary of the significant correlations is presented in Table 3.

Discussion

The current results support the initial hypothesis that a functional reorganization of basic cognitive functions is at the basis of mathematical performance in PA pediatric patients and compensate for eventual deficits caused by the tumor. In adults, the cerebellum has been most typically involved in motor or language functions [29], and more recently also in calculation tasks particularly under time constrains [3]. Based on the latter literature, it was reasonable to hypothesize negative effects on numerical and calculation tasks in pediatric patients with cerebellar PA. Conversely, at the group level, children with PA showed no significant impairments with respect to the control group of healthy children. These results point to some sort of neural compensation. In other words, because the tumor and its resection afflicted networks supporting math performance (e.g., the cerebellum and its connections), the brain necessitated and used additional compensatory functions to succeed in the mathematical tasks.

Based on the current results, it seems that such functional compensation in PA cerebellar patients was attained by means of visuomotor functions. Indeed, the mathematical performance of these patients was equivalent to that of the healthy control group, but the efficient execution of numerical tasks was associated to the visual working memory and visuomotor integration abilities in patients only. A correlation between numerical and visuomotor perceptual/integration abilities is generally reported in typically developing children about 6 to 7 years younger than those in the present study [4, 13, 14, 22, 26, 27]. In healthy children, such correlation becomes weaker throughout development, as the mathematics-related networks progressively get more specialized. The correlation of these functions in PA patients of about 11 years of age suggest either the maintenance or the reinstatement of primordial associations in order to successfully compensate for the missing cerebellar functions. Although these compensatory mechanisms become available to the patients without any specific rehabilitation program, it might be possible to hasten recovery by devising a comprehensive training of mathematics and cognitive abilities using multisensory modalities including visuomotor ones [12]. Such intervention might be able to impact on and strengthen the compensatory functions.

Determining the precise moment in which neural compensation begins is intriguing. It might have been triggered after the resection (explaining why patients become more efficient in performing some mathematical tests as the time from surgical resection to the neuropsychological examination increases) or even before the intervention by the mere presence of the tumor, the progressive shrinking of cerebellar tissues, and consequent reorganization of its functions during development. From a neurodevelopmental perspective, it is indeed plausible to hypothesize higher levels of neural compensation throughout development as the system consolidates alternative networks to achieve discrete levels of performance in response to the PA tumor grow before resection. This is congruent with the results showing that tumor size negatively correlated with the efficiency measures on numerical tasks (i.e., the bigger the tumor the faster the response times in numerical tests). This suggests a more efficient reconfiguration and higher levels of compensation in more developed tumors with respect to smaller ones. Tumor size is an important neurological outcome predictor also among other types of tumors [9], but future research should explore, among PA patients, whether it positively or negatively correlates with higher cognitive abilities—besides numerical ones—and whether the strength of the correlation could be modulated by factors such as age (by comparing for instance outcomes in children and adults whose levels of plasticity likely differ).

The performance of individual cases is worth discussing in order to explore the factors that modulate neuroplasticity in this type of patients. Four of the patients (Table 2) showed numerical difficulties in arithmetical tasks, e.g., additions and subtractions, and/or basic numerical tests such as dot-enumeration and magnitude comparison. In most of the cases, however, these difficulties were part of a more general cognitive impairment. Indeed, only two patients (patient 2 and patient 10) showed specific deficits in calculation tasks. Whether such difficulties were present independently of the tumor and its resection cannot be easily determined with the current data. It is possible that, because difficulties with mathematics are somewhat frequent among children, they might have been found fortuitously in this sample (independently of the clinical condition). Baseline measures of numerical or other neuropsychological abilities, which could have contributed to exclude this possibility, were not available at the time of the present research because in most of the cases, surgery was performed within 24-48 h from the admission. However, the correlational analysis showed that post-surgical mathematical abilities linearly improved with time (i.e., interval surgery-test), thus providing an indication that these functions were generally modulated by the presence and subsequent removal of the tumor. Patient 6 showed a performance significantly below that of controls in various neuropsychological and numerical tests. This suggests a general (non-specific to the numerical domain) cost of the presence of the tumor. The patient's general difficulties in the tasks could be attributed to his age (he was the youngest of the group), and to the mathematical skills that he has yet to learn.

Noticeably, specific pre-operative symptoms and the presence/absence of peri-operative complications (see Table 2) were neither necessary nor sufficient to determine a negative neuropsychological outcome. The presence of hydrocephalus was not predictive either of the successive mathematical performance of the children. In fact, from the patients that had hydrocephalus at the time of the diagnosis (9 out of 11), 6 showed no difficulties in numerical tasks.

The current findings should be interpreted in light of the limitation discussed above concerning the missing pre-operative data due to the retrospective nature of the study. Moreover, the group comparisons are based on a reduced sample size, which poses some constraints to the statistical power. The single case analyses are based on different statistical assumptions, however, and contribute to overcome these limitations (see effect size indexes in the Appendix). Future multisite studies that bring together samples from various clinical units should provide further elements and more robust statistical group comparisons for understanding and predicting the neurobehavioral outcomes in PA patients. Another limitation of the study concerns the timing of the neuropsychological assessment, which was variable and administered only in one occasion to all the participants. The findings indicated that such timing modulated the patients' responses in some mathematical tests and further suggests that structuring assessments at various time points (eventually including also some assessments before and after cognitive and mathematical training) could provide a better understanding of the progression of the recovery after surgical intervention.

To summarize, the present data suggest that PA does not necessarily cause cognitive or numerical impairments if properly resected at pediatric ages. In most of these patients, there seems to be a functional reestablishment of mathematical skills despite the presence of the tumor, the cerebellar violation, and the surgical manipulation. The reliance on visuomotor integration abilities to carry out specific mathematical tasks evidenced some compensatory mechanisms and suggest, at the same time, a modest trait of developmental delay in PA patients with respect to healthy peers that typically rely on visuomotor integration abilities to carry out mathematical tasks at younger ages.

Acknowledgments We wish to thank Laura Milanese for her valuable assistance on the recruitment of patients. Our gratitude also goes to the parents of all the children for their participation.

Funding This study was funded by the University of Padua (Grant Number: STPD11B88HM). The sponsor had no role in the design or conduct of this research.

Compliance with ethical standards

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

Ethical approval All procedures performed were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments.

Informed consent Informed consent was obtained from all individual participants included in the study.

References

1. Aarsen FK, Van Dongen HR, Paquier PF, Van Mourik M, Catsman-Berrevoets CE (2004) Long-term sequelae in children after cerebellar astrocytoma surgery. Neurology 62(8):1311–1316
2. Aarsen FK, Paquier PF, Arts WF, Van Veelen ML, Michiels E, Lequin M, Catsman-Berrevoets CE (2009) Cognitive deficits and predictors 3 years after diagnosis of a pilocytic astrocytoma in childhood. J Clin Oncol 27(21):3526–3532
3. Arsalidou M, Taylor MJ (2011) Is 2+2=4? Meta-analyses of brain areas needed for numbers and calculations. Neuroimage 54(3): 2382–2393
4. Barnhardt C, Borsting E, Deland P, Pham N, Vu T (2005) Relationship between visual-motor integration and spatial organization of written language and math. Optom Vis Sci 82(2):138–143
5. Benavides-Varela S, Burgio F, Meneghello F, De Marco M, Arcara G, Rigon J, Semenza C (2015) Anatomical substrates and neurocognitive predictors of daily numerical abilities in mild cognitive impairment. Cortex 71:58–67
6. Benavides-Varela S, Butterworth B, Burgio F, Arcara G, Lucangeli D, Semenza C (2016) Numerical activities and information learned at home link to the exact numeracy skills in 5–6 years-old children. Front Psychol 7
7. Bisiacchi PS, Cendron M, Gugliotta M et al (2005) BVN 5–11. Batteria di valutazione neuropsicologica per l'età evolutiva. Centro studi Erickson
8. Burgio F, Benavides-Varela S, Arcara G, Trevisson E, Frizziero D, Clementi M, Semenza C (2017) Numerical activities of daily living in adults with neurofibromatosis type 1. J Intellect Disabil Res 61(11):1069–1107
9. Chang SM, Parney IF, McDermott M, Barker FG, Schmidt MH, Huang W, Sloan AE (2003) Perioperative complications and neurological outcomes of first and second craniotomies among patients enrolled in the glioma outcome project. J Neurosurg 98: 1175–1181
10. Crawford JR, Garthwaite PH (2002) Investigation of the single case in neuropsychology: confidence limits on the abnormality of test scores and test score differences. Neuropsychologia 40:1196–1208
11. Daszkiewicz P, Maryniak A, Roszkowski M et al (2009) Long-term functional outcome of surgical treatment of juvenile pilocytic astrocytoma of the cerebellum in children. Childs Nerv Syst 25:855
12. Farghaly WM, Ahmed MA, El-Tallawy HN et al (2018) Construction of an Arabic computerized battery for cognitive rehabilitation of children with specific learning disabilities. Neuropsychiatr Dis Treat 14:2123
13. Friso-van den Bos I, Van der Ven SHG, Kroesbergen EH, Van Luit JEH (2013) Working memory and mathematics in primary school children: a meta-analysis. Educ Res Rev 10:29–44
14. Geary DC (1993) Mathematical disabilities: cognitive, neuropsychological, and genetic components. Psychol Bull 114(2):345
15. Gupta N, Banerjee A, Haas-Kogan D (2004) Pediatric CNS tumors. Springer-Verlag, Heidelberg
16. Kirschen MP, DavisRatner MS, Milner MW, Chen SH, Schraedley Desmond P, Fisher PG, Desmond JE (2008) Verbal memory impairments in children after cerebellar tumor resection. Behav Neurol 20:39–53
17. Konczak J, Schoch B, Dimitrova A, Gizewski E, Timmann D (2005) Functional recovery of children and adolescents after cerebellar tumor resection. Brain 128:1428–1441
18. Lis A, Di Nuovo S (1982) Test della grande figura complessa di Rey traduzione italiana. Organizzazioni Speciali, Firenze
19. Mammarella IC, Toso C, Pazzaglia F, Cornoldi C (2008) BVS-Corsi. Batteria per la valutazione della memoria visiva e spaziale. Con CD-ROM. Edizioni Erickson
20. Morgan AT, Liegeois F, Liederkerke C, Vogel AP, Hayward R, Harkness W et al (2011) Role of cerebellum in fine speech control in childhood: persistent dysarthria after surgical treatment for posterior fossa tumour. Brain Lang 117(2):69–76
21. Noone AM, Howlader N, Krapcho M, Miller D, Brest A, Yu M, Ruhl J, Tatalovich Z, Mariotto A, Lewis DR, Chen HS, Feuer EJ, Cronin KA (eds). SEER Cancer Statistics Review, 1975–2015, National Cancer Institute. Bethesda, MD, based on November 2017 SEER data submission, posted to the SEER web site, April 2018. https://seer.cancer.gov/csr/1975_2015/
22. Pieters S, Desoete A, Roeyers H, Vanderswalmen R, Van Waelvelde H (2012) Behind mathematical learning disabilities: what about visual perception and motor skills? Learn Individ Differ 22(4):498–504
23. Preda C (2015) VMI Developmental test of visual-motor integration: Il Beery-Buktenica con i test supplementari di percezione visiva e coordinazione motoria: manuale. Organizzazioni Speciali, Firenze
24. Reigosa-Crespo V, Valdés-Sosa M, Butterworth B, Estévez N, Rodríguez M, Santos E, Lage A (2012) Basic numerical capacities and prevalence of developmental dyscalculia: the Havana survey. Dev Psychol 48(1):123
25. Scarpa P, Piazzini A, Pesenti G et al (2006) Italian neuropsychological instruments to assess memory, attention and frontal functions for developmental age. Neurol Sci 27(6):381–396
26. Solan HA, Mozlin R, Rumpf DA (1985) The relationship of perceptual-motor development to learning readiness in kindergarten a multivariate analysis. J Learn Disabil 18(6):337–344
27. Sortor JM, Kulp MT (2003) Are the results of the Beery-Buktenica developmental test of visual-motor integration and its subtests related to achievement test scores? Optom Vis Sci 80(11):758–763
28. Steinlin M, Imfeld S, Zulauf P, Boltshauser E, Lovblad KO, Ridolfi-Luthy A, Perrig W, Kaufmann F (2003)

Neuropsychological long term sequelae after posterior fossa tumour resection during childhood. Brain 126:1998–2008
29. Stoodley CJ, Schmahmann JD (2009) Functional topography in human cerebellum: a meta-analysis of neuroimaging studies. Neuroimage 44(2):489–501
30. Wechsler D (2012) Wechsler preschool and primary scale of intelligence—fourth edition. Pearson Assessments, San Antonio

Comments

The authors review a cohort of 11 children with pilocytic astrocytoma of the cerebellum and administer a battery of neuropsychological and mathematical tests between 0.6 and 5.5 years after surgical resection. The same tests are also carried out with a group of matched controls. The authors find recovery of mathematical ability in all patients. They also find that visuospatial memory and visual-motor integration were associated with mathematical skills in patients only. Mathematical skills also correlated with time from surgery and, inversely, with size of the tumor. They conclude that the recovery and emergence of mathematical skills in patients are supported by the reorganisation of visuospatial and visual-motor skills, replicating processes that typically occur in younger children.

This is an interesting concept and reflects not just the ability of these children to recover their mathematical skills after surgery but also underlines the importance of the cerebellum in cognitive development.

Kristina Aquilina
London, UK