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Running title: Cognitive performance of medulloblastoma survivors

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Abstract

Background: The aim of the study was to determine the relationship between a damaged cerebellum area and the cognitive performance of medulloblastoma tumour survivors. Also, age-based differences in cognitive performance were tested.

Materials and methods: Magnetic resonance imaging (MRI) technique was used to obtain brain images of survivors. The cognitive performance was tested using Wechsler Intelligence Scale for Children Revised (WISC-R) and Wechsler Adult Intelligence Scale (WAIS). Statistical analysis was performed with highly robust permutation tests.

Results: There were two anatomical features strongly influencing the cognitive performance of survivors. The extension of the foramen of Luschka had a negative impact on the overall verbal IQ score and some non-verbal scales while the excision of the middle part of the vermis influenced scores in such scales as arithmetic and picture completing.

Conclusions: Children with postoperative damages in the area of the middle part of the vermis are more likely to suffer from cognitive dysfunctions after the end of the treatment.

Keywords: medulloblastoma; cognitive performance; cerebellum; MRI

Background

In connection with the increasing number of cancer patients and greater survivor ratio, increasingly, researchers are interested in long-term sequelae of both cancer and cancer treatment. Usage of multidimensional and specialized treatment, including surgery and recent chemotherapy and radiotherapy protocols, lead to the growth in the number of child cancer survivors who are vulnerable to negative late effects of applied therapies. The effects concern up to 62% of child patients treated for cancers. The children with the most complications are those treated for central nervous system (CNS) tumours [1]. Brain tumours are the second most common form of childhood cancer, following leukaemia, comprising 20% of new diagnoses [2,3].

Childhood brain tumour (BT) survivors are at increased risk for cognitive impairments because of disease and treatment-related factors [2, 4–6]. Research suggests that attention [7,8], working memory disorders [9] and lower general IQ might occur as the most crucial long-term cognitive symptoms [4, 10–12].

Ris et al. [13] in their longitudinal study, indicated that a decline in IQ level reached up to 17.4 points on the Wechsler scale four years after radiotherapy. Hoppe-Hirsch et al. [14] provide similar data from five years follow-up because 42% of patients were found to have an IQ lower than 80. Craniospinal irradiation (CSI) doses, younger age at the time of treatment, and time since treatment seem to be the crucial factors for patients' mental development [4, 13]. Much research shows that IQ scores are related to the failure to make age-appropriate gains over time, as opposed to actual loss of skills [15, 16].

Localization and size of the tumour are also vital factors for cognitive performance [16, 17]. Children with infratentorial tumours, like medulloblastoma, usually have a greater cognitive load than those with supratentorial tumours [16]. This is related to the frequent occurrence (70–80% cases) of obstructive hydrocephalus, which constricts the flow of cerebrospinal fluid.

The most frequent negative aftermath of neurochirurgical procedures is posterior fossa syndrome [18] also known as cerebellar mutism, which occurs in up to 31% of children with infratentorial tumours. These disorders present 24–48 hours after surgery but usually improve

over time when appropriate rehabilitation is used [16]. Some research indicates an overall lower level of performance in cognitive tasks when this syndrome occurs [19].

The aim of the present study was to identify the anatomical structures where damage could be linked to the cognitive function of children with medulloblastoma. The hypothesis was that damage to the medial structures (vermis cerebelli) was a strong predictor of cognitive outcome.

Material and methods

Participants

13 participants between 4 and 17 years old at the time of diagnosis were included in this study. Eligibility criteria required for participants to have completed oncological treatment, at the time of examination, be in complete remission, preferably 3 years or more after the end of the therapy. Three subjects did not meet the 3-year-post-treatment criterion, and were included based on the remaining conditions. The study was approved by the Institutional Review Board. Written informed consent was required prior to participation.. The mean age at the time of examination was 16.64 (range 7.00–26.00). The mean time of diagnosis was 9.67 years (range 4.00–17.00 years). The mean follow-up time after the completion of treatment was 6.64 years (range 1.00–10.00 years) in Table 1.

Table 1. Demographic characteristic of participants

ID	**Sex**	**Age at diagnosis**	**Age at the end of treatment**	**Range of treatment years**	**Range of follow-up time**	**Age at examination**	**Risk group**
Subject1	Female	9.5	10.5	1	4.5	15	SR
Subject2	Female	16	18	2	2	20	HR
Subject3	Female	4,5	7	2.5	6	13	HR
Subject4	Male	17	19	2	6	25	SR
Subject5	Male	9.5	11	1.5	10	21	SR
Subject6	Male	8	9.5	1.5	5.5	15	SR
Subject7	Female	4	5.5	1,5	2.5	8	HR
Subject8	Female	7.5	10	2.5	1	10	HR

Subject9	Male	12.5	14	1.5	7	21	HR
Subject10	Female	17	18.5	1.5	5.5	24	HR
Subject11	Male	6	7	1	10	17	HR
Subject12	Male	16.5	17.5	1	7.5	25	SR
Subject13	Male	4	5	1	2	7	HR

SR — standard risk; HR — high risk

Procedure of treatment

Treatment of all children was conducted according to the Standardized Brain Tumours Treatment Protocol applied in Poland. Initially, patients undergo a surgical procedure to mechanically reduce the mass of the tumour and to obtain material for histopathological assessment. Only patients with diagnosed medulloblastoma tumours were included in further study. Children were classified into two risk groups: standard risk (SR) and high risk (HR). These groups were based on stratifying factors such as histopathological type of medulloblastoma, size of excised tumour tissue during surgical procedure documented by MRI, presence of metastases in the brain or spinal cord, and presence of cancer cells in cerebrospinal fluid. Anaplastic type of tumour, leaving more than 1 cm^3 of cancer tissue in the first procedure and presence of metastases, qualified the patient to the HR group. This group assignment was related to more aggressive chemotherapy, higher doses of radiotherapy, and longer postsurgical treatment.

Radio- and chemotherapy

Chemoradiotherapy (CRT), including intensity-modulated radiation therapy, was delivered over 6 weeks with a prescribed dose of 24 Gy/13 fractions on CNS and boost to whole posterior fossa (or tumour bed): 54 Gy/30 fractions in SR group and 36 Gy on CNS, 54 Gy/13 fractions and boost to whole posterior fossa (or tumour bed in HR group). All children after surgery received 4 cycles of chemotherapy, depending on their weight. After radiotherapy 5 (SR group) to 8 (HR group) chemotherapy cycles were applied as well.

MRI measures

All children had an MRI examination at the end of treatment. The protocol contained T2 FLAIR, diffusion-weighted imaging (DWI), diffusion tensor imaging (DTI) and 3D BRAVO sequences in the transversal plane and 3D CUBE FLAIR sequence in the sagittal plane.

The morphological data analysis included the following:

- evaluation of tumour bed volume and extension of the IV ventricle of the brain;
- division of the cerebellum into three areas containing such main anatomical structures as the vermis, intermediate zone of the cerebellum, and lateral zone of the cerebellum; the aim was to assess the range of postprocedural and post-therapeutic changes;
- volume symmetry evaluation of cerebellum hemispheres and cerebellum limbs;
- evaluation of the foramen of Luschka extension;
- evaluation of water flow disorders in DWI sequence correlated with late phase (at least 3 years after treatment) apparent diffusion coefficient (ADC) map;
- evaluation of fibres distribution and symmetry in DTI;
- detailed evaluation of excised structural fragments;
- evaluation of accompanying signal disorders, especially gliosis.

Cognitive assessment

The intelligence tests used were the Wechsler Intelligence Scale for Children Revised (WISC-R) and the Wechsler Adult Intelligence Scale (WAIS). Both instruments are well-validated, belong to the same group of tools, and assess widely used measures of cognitive ability. Composites and IQ scores were converted to a common standard score (M = 100; SD = 15).

Statistical analysis

The analysis was conducted with the R language and RStudio [20]. To import the data, the readxl package was used. To manage the data, we used dplyr, tidyr, magrittr, and openxlsx packages. For computing, we used the coin package with permutation tests, rstatix, and psych.

The study's database consisted of two parts. The first contained anatomical data from magnetic resonance imaging (MRI) and the second contained cognitive data. In addition, socio-demographic data such as sex and age were entered.

Descriptive statistics were calculated for the continuous variables: cognitive data, tumour bed volume (TBV), the age at diagnosis, and cognitive performance indicators (Supplementary File — Table S1). Furthermore, Shapiro-Wilk's tests of normality were performed. For the rest of the MRI data, which includes only nominal variables, sample size and percentages were computed (Supplementary File — Tab. S1).

To test the experimental hypothesis concerning the relationship between anatomical features and the cognitive performance of survivors, statistical analysis was performed. Owing to the small sample sizes, highly robust permutation tests of independence [22] were used to determine differences between groups (Supplementary File — Tab. S2). The conditional null distribution was approximated by Monte Carlo resampling [23]. To determine the effect size, Cohen's *d* coefficient was calculated [24].

Results

Two strong discriminative factors were discovered. The first was the extension of the foramen of Luschka Table 1, and the second was the excision of the middle part of the vermis depicted in Figure 1, Table 2.

The extension of the foramen of Luschka and the excision of the middle part of the vermis were both correlated with the lower cognitive performance of survivors (Tab. 2 and 3), But also associated was the younger age at diagnosis of medulloblastoma (Tab. 4).

According to the standards of interpretation provided by Cohen [24], Cohen's *d* coefficient suggests big effect sizes in all presented cases.

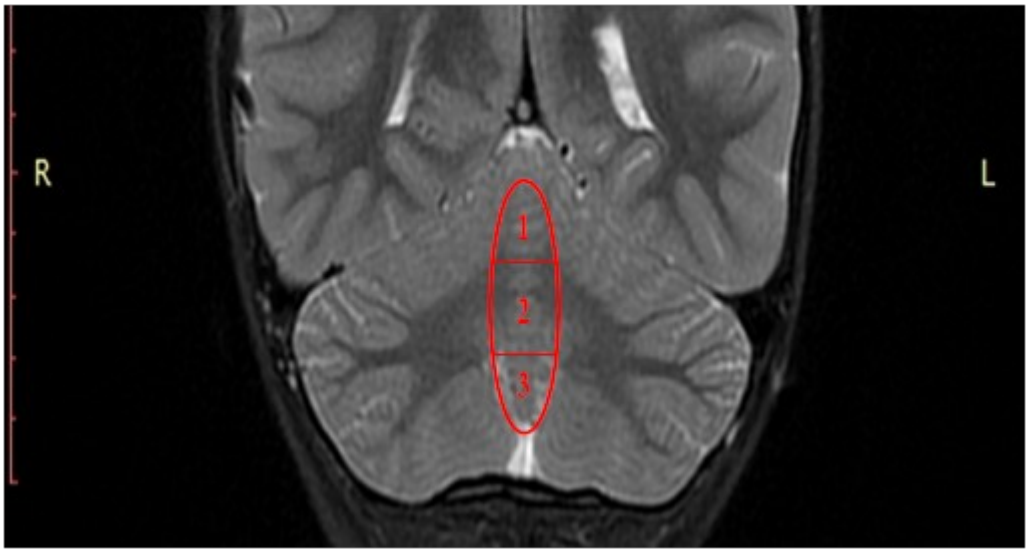

Figure 1. Division of the vermis: 1 — upper part, 2 — middle part, 3 — lower part

Table 2. Significant permutation independence tests for Wechsler Intelligence Scale for Children (WISC), similarities and picture ordering

Variable	**Foramen of Luschka extended**				**Z**	**p**	**Cohen's d**
	No		**Yes**				
	M	**SD**	**M**	**SD**			
IQ verbal	101.71	18.78	78.80	13.46	1.96	0.048	-1.49
IQ performance	103.29	14.75	82.20	25.99	1.64	0.100	–1.15
IQ full	105.33	12.40	76.00	20.58	2.13	0.028	–2.05
Similarities	12.00	2.58	7.00	3.67	2.19	0.020	–1.79
Pictures ordering	11.43	3.10	7.00	3.39	1.98	0.048	–1.51
Age of diagnosis	11.79	5.33	6.70	2.66	1.74	0.091	1.21
End of treatment	13.43	5.22	8.10	2.56	1.83	0.066	1.30

M — mean; SD — standard deviation; Z — measures the distance between a data point and M using SD; Cohen d — effect size measurement

Table 3. Significant permutation independence tests for arithmetic, picture completing, age of diagnosis and age at the end of treatment

Variable	**The middle part of the**	**Z**	**p**	**Cohen's**

	vermis excised						d
	No		Yes				
	M	SD	M	SD			
IQ verbal	110.00	4.00	86.22	19.58	1.79	0.078	1.68
IQ performance	114.00	6.00	88.00	21.54	1.78	0.065	1.64
IQ full	112.00	5.57	85.71	20.78	1.78	0.066	1.73
Arithmetics	12.00	1.00	5.89	4.11	2.05	0.034	–1.81
Pictures completing	14.33	1.53	8.44	3.47	2.19	0.023	–2.03
Age of diagnosis	15.50	2.60	7.72	3.95	2.34	0.010	–2.29
End of treatment	17.17	2.75	9.22	3.80	2.39	0.010	–2.41

M — mean; SD — standard deviation; Z — measures the distance between a data point and M using SD Cohen d — effect size measurement

Table 4. The results of one sample t-student tests for two age groups based on the control values provided by Ryan et al. [25]

Variable	Tested value	≤ 8.5 years old			> 8.5 years old		
		M	SD	p	M	SD	p
Similarities	10.20	9.33	2.66	0.461	10.50	5.05	0.890
Vocabulary	10.48	6.67	3.72	0.054	9.67	3.27	0.569
Information	10.25	7.17	3.31	0.071	9.00	4.38	0.516
Block design	10.30	8.50	4.23	0.345	8.33	4.50	0.333
Visual puzzles	10.52	11.50	2.67	0.409	9.83	2.64	0.552
Digit span	10.60	9.50	3.73	0.502	10.83	2.93	0.853
Arithmetic	10.43	5.00	2.68	0.004	9.83	4.79	0.773
Coding	10.78	5.83	3.31	0.015	9.17	5.23	0.484

M — mean; SD — standard deviation

Analysing the results presented in Table 4 we can see no statistically significant difference in cognitive performance between children with an age at diagnosis higher than 8.5 and the standard norm. In children with an age at diagnosis less than 8.5 years significant or nearly significant differences were seen in two verbal subscales and one nonverbal subscale, as follows:

- arithmetic, a verbal task that measures immediate memory and focus; requires the ability to perform mathematical calculations. The examiner reads a mathematical problem and the individual is required to complete the calculation without the use of paper and pencil. Arithmetic measures attention and memory, but also requires quick recall of math facts and functions and general proficiency in basic math calculations. No visual information or motor response is required;
- vocabulary, a test that measures word knowledge and the ability to verbally express the definition of words. Words are presented both visually (in large print) and orally to the student. This task requires minimal receptive and expressive vocabulary and no motor response is required. An appropriate definition can be a single word (synonym). The questions tend to tap information and experience learned through daily life and in the classroom. Disorders in this field can indicate impaired knowledge acquisition;
- coding, visual, paper and pencil tasks requiring individuals to match numbers with symbols based on a key at the top of the page by drawing the correct symbol in the boxes provided. Coding measures visual processing speed, short-term visual memory, and the ability to shift eye gaze efficiently back and forth between the key and the responses. This task requires fine motor skills (using a pencil) but does not require expressive language. Minimal demands are placed on receptive language. It also assesses the ability to sustain focus for two minutes.

Discussion

Children who have been treated for a malignant posterior fossa tumour (PFT) are at risk of intellectual impairment. Cerebellar deficits caused by the tumour and medical procedures, especially radio- and chemotherapy, have a strong impact on intellectual performance. It is worth mentioning that beyond the localisation and volume of the tumour, the crucial factor is also postoperative cognitive dysfunction — POCD) [26]. It has not an official definition, but some authors claim that this consists of cognitive impairment of one or several functions, which results in e.g. attention disorders [7,8], working-memory disorders [9] and lower general IQ [4], occurring past surgical and others medical procedures. It can last from several days to months [27] and can be caused by the damage of neural connections between the cerebellum and encephalon which are responsible for cognitive performance. The group especially vulnerable to long-term effects of treatment in our study are children with an age at diagnosis lower than 8.5, similarly to [28]. Such children have lower verbal abilities, such as immediate memory, focus, word knowledge, and giving the definition of words.

Worse functioning could be observed also in performance ability, such as visual-processing speed and short-term visual memory.

In the DWI, DTI, and MRI procedures such anatomical structures as the vermis, foramen of Luschka, and gliosis were examined. Especially, the middle part of the vermis and extension of the foramen of Luschka were of significance. Other features, such as the location of the tumour, did not differentiate the level of cognitive performance in the examined group, in contrast to the previous studies [29, 30]. Differences can be caused by the differences in examination time. Our patients were examined for cognitive performance at a minimum of 3 years after the end of the treatment, whereas Riva [29] made the measurements during the treatment and Puget et al. [30] at least 6 months after the end of the treatment. So, we can assume, at an early stage, that the location of the tumour in the left or right side of the cerebellum can negatively affect cognitive functions but, with the passage of time, children effectively compensate for this decline. To test this hypothesis, a longitudinal study should be conducted, beginning at the end of treatment up to 6–7 years after the end of the treatment, to determine if the compensation effect occurs systematically.

The lack of the foramen of Luschka is so essential for the cognitive functioning of survivors that, even after the passage of time after treatment, it still differentiates patients. This area especially affects the general IQ level, both verbal and nonverbal. The largest difference above one SD appears in nonverbal intelligence, which indicates difficulties in knowledge acquisition. Significant differences were also noted in two subscales (similarities, picture ordering) of verbal intelligence. The key abilities in both these tasks are reasoning and compartmentalization. It is also worth mentioning that the age of the children is correlated with cognitive performance after the end of the treatment: the younger the children, the worse the cognitive performance, especially in verbal intelligence. Younger children (range at surgery: 4–8 years old) had the lowest scores in semantic fluency and, consequently, showed the most difficulty in verbal intelligence.

The second significant area was the middle part of the vermis. Damage of this area concerned younger children (M = 7.72) most often. This relationship can result from the fact that tumour often occurs in the inferior and middle part of the vermis and, in young children, these structures are so small that resection with margins hooks this field. Puget et al. [30] obtained similar results, although they indicated more firmly the inferior part of the vermis

Limitations of the study

The study is a cross-sectional analysis. Our sample size was limited and three subjects did not meet the 3-year-period criterion There is a need to replicate the study in a bigger sample, which will enable subgroup analyses.

The second limitation is that this study is restrained to one country whose sociocultural heritage and quality of healthcare system may have influenced participants' responses, therefore, limiting the generalizability of the results to other nations that differ significantly from Poland for the aforementioned variables.

In addition, the effect of radiation on the cognitive impairment could not be controlled, as the standard procedure assumed a surgical procedure as well as radiotherapy. Thus, the assignment of a control group was ethically impossible.

Clinical implications

The study provides insight into the effect of childhood neoplasm on the cognitive performance of survivors. An accurate assessment of a child's cognitive performance at different stages of treatment and recovery contributes to care planning and matching them with tailored support services.

Based on these results, we suggest that further intervention or qualitative studies explore whether therapeutic interventions directed towards the support of cognitive development could lead to long-term improvement.

Conclusions

Cerebellar damage plays a major role in cognitive impairment in children with posterior fossa tumours. Children with postoperative and persistent cerebellar deficits are at risk for impaired intellectual outcome and deserve special education measures as soon as possible after the completion of cancer treatment. During surgery of younger children (especially below 8), special care during resection should be taken in the area of the middle and inferior part of the vermis, because any damage can cause negative effects difficult to rehabilitate. Evaluating children three years after treatment, however, resulted in improvement in many cognitive functions.

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Conflict of interests

The authors declare no conflicts of interests.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethical approval statement

The advice of the Internal Review Board of the Medical University of Silesia in Katowice so as to the need of submitting a formal application for study protocol approval was sought prior to the commencement of this study. The IRB approved the study as a non-interventional one. Reference number for the approval : KNW/022/KB/49/15.

Patient consent statement

Every participant expressed written, informed consent before the beginning of the study.

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Supplementary File

Table S1. Descriptive statistics for continuous variables

Variable	n	M	SD	95% CI		Me	IQR	Min	Max	Sk.	Kurt.	W	p
				Lower	Upper								
Tumour bed volume	13	6.49	3.26	4.78	8.19	5.01	1.86	3.20	14.70	1.45	0.56	0.80	0.007
Age at	11	16.6	6.86	13.04	20.23	15.00	11.0	7.00	26.00	0.07	–	0.92	0.32

evaluation		4					0				1.60		0
Age of diagnosis	12	9.67	4.99	7.05	12.28	8.75	7.88	4.00	17.00	0.43	–1.52	0.88	0.083
Age at the end of treatment	12	11.21	4.98	8.60	13.82	10.25	7.88	5.00	19.00	0.42	–1.47	0.91	0.188
Age at the beginning of the treatment	12	17.67	6.95	14.03	21.31	17.00	10.25	7.00	27.00	–0.13	–1.56	0.94	0.457
Treatment time	12	6.46	3.38	4.69	8.23	7.00	4.38	1.00	12.00	–0.18	–1.26	0.96	0.749
WISC verbal	12	92.17	19.94	81.72	102.61	94.00	31.00	64.00	123.00	–0.14	–1.48	0.94	0.511
WISC nonverbal	12	94.50	21.96	83.00	106.00	105.50	33.25	55.00	120.00	–0.63	–1.37	0.88	0.099
WISC full	10	93.60	21.36	82.41	104.79	98.50	27.50	59.00	117.00	–0.58	–1.36	0.89	0.182
Knowledge	12	08.08	3.83	06.08	10.09	9.50	5.75	1.00	12.00	–0.59	–1.33	0.89	0.132
Similarities	12	9.92	3.90	7.88	11.96	10.00	6.25	1.00	14.00	–0.79	–0.25	0.87	0.062
Arithmetics	12	7.42	4.48	05.07	9.76	8.00	7.25	1.00	14.00	–0.02	–1.52	0.94	0.438
Dictionary	12	8.17	3.69	6.23	10.10	9.50	6.25	2.00	14.00	–0.25	–1.41	0.93	0.383
Understanding	12	10.25	3.82	8.25	12.25	10.00	6.25	3.00	15.00	–0.30	–1.26	0.93	0.359
Number	12	10.1	3.27	8.45	11.88	10.50	4.50	4.00	15.00	–	–	0.97	0.94

repeating		7								0.29	1.17		0
Pictures completing	12	9.92	04.03	7.80	12.03	10.00	3.75	1.00	16.00	–0.66	–0.35	0.96	0.759
Pictures ordering	12	9.58	3.83	7.58	11.59	9.50	3.25	2.00	17.00	0.00	–0.30	0.97	0.924
Bricks patterns	12	8.42	4.17	6.23	10.60	10.50	5.25	1.00	13.00	–0.86	–1.06	0.84	0.026
Puzzles	12	10.67	2.67	9.27	12.07	11.00	3.25	6.00	16.00	0.14	–0.67	0.97	0.914
Coding	12	7.50	4.52	5.13	9.87	8.00	7.00	1.00	14.00	0.04	–1.61	0.94	0.436

Table S1. Remaining results of statistical analysis; grouping factor in the second column

Dependent variable	**Group**	**No***		**Yes***		**Z**	**p**
		M	**SD**	**M**	**SD**		
WISC verbal	Vermis excised	94.67	26.86	91.33	19.05	0.25	0.811
	Part of vermis excised	94.67	26.86	87.2	16.71	0.73	0.766
	Upper part of vermis excised	90	19.51	96.5	23.06	–0.53	0.621
	Middle part of vermis excised	110	4	86.22	19.58	1.79	0.078
	Lower part of vermis excised	91.33	13.65	92.44	22.35	–0.08	0.951

	Intermediate zone of the cerebellum excised	91.1	21.5	97.5	12.02	–0.41	0.717
	Accompanying changes	101	–	91.36	20.7	0.46	0.749
	Gliosis	100	10.54	89.56	22.09	0.79	0.461
	Foramen of Luschka extended	101.71	18.78	78.8	13.46	1.96	0.048
	DTI asymmetry	95	19.07	90.14	21.79	0.42	0.681
	DTI asymmetry: site with more volume	89	8.72	91	29.94	–0.12	0.884
	Cerebellum symmetry	90.14	21.79	95	19.07	–0.42	0.696
WISC nonverbal	Vermis excised	96.67	30.62	93.78	20.65	0.2	0.861
	Part of vermis excised	96.67	30.62	96.8	18.73	0.5	0.88
	Upper part of vermis excised	96.75	21.64	90	25.21	0.5	0.647
	Middle part of vermis excised	114	6	88	21.54	1.78	0.065

	Lower part of vermis excised	96.67	18.77	93.78	23.93	0.2	0.855
	Intermediate zone of the cerebellum excised	95.1	22.95	91.5	23.33	0.21	0.866
	Accompanying changes	89	–	95	22.96	–0.26	1
	Gliosis	92.67	19.76	95.11	23.75	–0.17	0.89
	Foramen of Luschka extended	103.29	14.75	82.2	25.99	1.64	0.1
	DTI asymmetry	100.4	18.09	90.29	24.82	0.79	0.46
	DTI asymmetry: site with more volume	99	18.36	83.75	29.58	0.8	0.436
	Cerebellum symmetry	90.29	24.82	100.4	18.09	–0.79	0.463
WISC full	Vermis excised	94	30.81	93.43	19.17	0.04	0.974
	Part of vermis excised	94	30.81	94	16.52	0.07	0.995
	Upper part of vermis excised	94	22.11	93	23.51	0.07	0.936

	Middle part of vermis excised	112	5.57	85.71	20.78	1.78	0.066
	Lower part of vermis excised	94.5	16.26	93.38	23.42	0.07	0.98
	Intermediate zone of the cerebellum excised	93.38	23.42	94.5	16.26	–0.07	0.978
	Accompanying changes	95	–	93.44	22.64	0.07	1
	Gliosis	97	15.1	92.14	24.49	0.33	0.778
	Foramen of Luschka extended	105.33	12.4	76	20.58	2.13	0.028
	DTI asymmetry	100.25	14.59	89.17	25.18	0.8	0.435
	DTI asymmetry: site with more volume	94	11.31	86.75	31.48	0.33	0.741
	Cerebellum symmetry	89.17	25.18	100.25	14.59	–0.8	0.437
Knowledge	Vermis excised	7.67	5.86	8.22	3.38	–0.22	0.861
	Part of vermis excised	7.67	5.86	6.4	3.51	1.55	0.287

	Upper part of vermis excised	6.88	4.16	10.5	1.29	–1.55	0.137
	Middle part of vermis excised	11.33	1.15	7	3.81	1.7	0.1
	Lower part of vermis excised	7.67	2.08	8.22	4.35	–0.22	0.864
	Intermediate zone of the cerebellum excised	8	4.16	8.5	2.12	–0.17	0.911
	Accompanying changes	11	–	7.82	3.89	0.8	0.582
	Gliosis	10	2.65	7.44	4.07	1	0.355
	Foramen of Luschka extended	9.14	3.93	6.6	3.51	1.14	0.308
	DTI asymmetry	8.8	3.27	7.57	4.35	0.55	0.613
	DTI asymmetry: site with more volume	6.33	3.51	8.5	5.2	–0.65	0.6
	Cerebellum symmetry	7.57	4.35	8.8	3.27	–0.55	0.608
Similarities	Vermis excised	8.33	6.66	10.44	2.92	–0.81	0.494

	Part of vermis excised	8.33	6.66	9.8	2.68	0.84	0.725
	Upper part of vermis excised	9.25	4.17	11.25	3.4	–0.84	0.489
	Middle part of vermis excised	12.67	2.31	9	3.97	1.41	0.22
	Lower part of vermis excised	9	1.73	10.22	4.44	–0.47	0.645
	Intermediate zone of the cerebellum excised	9.9	4.31	10	0	–0.03	1
	Accompanying changes	14	–	9.55	3.86	1.09	0.416
	Gliosis	12.67	2.31	9	3.97	1.41	0.225
	Foramen of Luschka extended	12	2.58	7	3.67	2.19	0.02
	DTI asymmetry	11.2	2.68	9	4.55	0.96	0.413
	DTI asymmetry: site with more volume	9	1.73	9	6.27	0	1
	Cerebellum symmetry	9	4.55	11.2	2.68	–0.96	0.408

Arithmetics	Vermis excised	8.33	6.43	7.11	4.11	0.41	0.706
	Part of vermis excised	8.33	6.43	7.2	3.35	0.41	0.92
	Upper part of vermis excised	7.63	4.31	7	5.48	0.23	0.85
	Middle part of vermis excised	12	1	5.89	4.11	2.05	0.034
	Lower part of vermis excised	9	1.73	6.89	5.06	0.71	0.552
	Intermediate zone of the cerebellum excised	7	4.78	9.5	2.12	–0.72	0.526
	Accompanying changes	5	–	7.64	4.63	–0.56	0.749
	Gliosis	8.33	3.51	7.11	4.91	0.41	0.713
	Foramen of Luschka extended	9	4.47	5.2	3.83	1.45	0.165
	DTI asymmetry	8.2	3.83	6.86	5.11	0.51	0.664
	DTI asymmetry: site with more volume	6.67	2.31	7	6.98	–0.09	0.881

	Cerebellum symmetry	6.86	5.11	8.2	3.83	–0.51	0.659
Dictionary	Vermis excised	8.33	3.79	8.11	3.89	0.09	1
	Part of vermis excised	8.33	3.79	7.2	3.96	0.77	0.78
	Upper part of vermis excised	7.63	3.66	9.25	4.03	–0.72	0.526
	Middle part of vermis excised	10.33	0.58	7.44	4.03	1.17	0.307
	Lower part of vermis excised	7.67	3.21	8.33	4	–0.27	0.853
	Intermediate zone of the cerebellum excised	7.9	4.01	9.5	0.71	–0.56	0.622
	Accompanying changes	11	–	7.91	3.75	0.8	0.675
	Gliosis	10	1	7.56	4.1	0.99	0.399
	Foramen of Luschka extended	9.86	3.72	5.8	2.17	1.88	0.065
	DTI asymmetry	8.6	3.78	7.86	3.89	0.34	0.758

	DTI asymmetry: site with more volume	7.33	3.51	8.25	4.65	–0.31	0.798
	Cerebellum symmetry	7.86	3.89	8.6	3.78	–0.34	0.759
Understanding	Vermis excised	13.67	1.15	9.11	3.72	1.79	0.091
	Part of vermis excised	13.67	1.15	9.6	3.29	1.79	0.183
	Upper part of vermis excised	11.13	3.31	8.5	4.65	1.12	0.319
	Middle part of vermis excised	12	1.73	9.67	4.21	0.92	0.404
	Lower part of vermis excised	9.67	3.06	10.44	4.19	–0.31	0.771
	Intermediate zone of the cerebellum excised	10.3	3.97	10	4.24	0.1	1
	Accompanying changes	10	–	10.27	4	–0.07	1
	Gliosis	9	1.73	10.67	4.3	–0.65	0.591
	Foramen of Luschka extended	11.71	2.81	8.2	4.38	1.57	0.128
	DTI asymmetry	10	3	10.43	4.54	–0.19	0.871

	DTI asymmetry: site with more volume	10.33	4.16	10.5	5.45	–0.05	1
	Cerebellum symmetry	10.43	4.54	10	3	0.19	0.872
Number repeating	Vermis excised	10	2.65	10.22	3.6	–0.1	1
	Part of vermis excised	10	2.65	10.6	2.41	0.39	0.931
	Upper part of vermis excised	10.38	2.33	9.75	5.12	0.31	0.788
	Middle part of vermis excised	11.67	0.58	9.67	3.67	0.92	0.433
	Lower part of vermis excised	11.33	3.06	9.78	3.42	0.71	0.562
	Intermediate zone of the cerebellum excised	10.2	3.49	10	2.83	0.08	1
	Accompanying changes	4	–	10.73	2.76	–1.97	0.086
	Gliosis	8	4	10.89	2.89	–1.32	0.24
	Foramen of Luschka extended	10.43	3.41	9.8	3.42	0.33	0.799
	DTI asymmetry	8.8	3.11	11.14	3.24	–1.22	0.258

	DTI asymmetry: site with more volume	12.33	2.08	10.25	3.95	0.84	0.426
	Cerebellum symmetry	11.14	3.24	8.8	3.11	1.22	0.261
Pictures completing	Vermis excised	12	5.29	9.22	3.63	1.03	0.337
	Part of vermis excised	12	5.29	10.4	2.41	1.32	0.438
	Upper part of vermis excised	11	3.46	7.75	4.72	1.32	0.215
	Middle part of vermis excised	14.33	1.53	8.44	3.47	2.19	0.023
	Lower part of vermis excised	11.67	2.52	9.33	4.39	0.87	0.438
	Intermediate zone of the cerebellum excised	9.6	4.22	11.5	3.54	–0.61	0.596
	Accompanying changes	9	–	10	4.22	–0.24	1
	Gliosis	10.33	2.31	9.78	4.58	0.21	0.872
	Foramen of Luschka extended	11.29	3.2	8	4.64	1.39	0.175
	DTI asymmetry	11.8	3.11	8.57	4.28	1.37	0.216

	DTI asymmetry: site with more volume	10.33	2.89	7.25	5.06	0.94	0.491
	Cerebellum symmetry	8.57	4.28	11.8	3.11	–1.37	0.205
Pictures ordering	Vermis excised	10.67	3.51	9.22	4.06	0.57	0.597
	Part of vermis excised	10.67	3.51	10.2	4.21	1.01	0.632
	Upper part of vermis excised	10.38	3.7	8	4.08	1.01	0.366
	Middle part of vermis excised	12	1.73	8.78	4.06	1.26	0.25
	Lower part of vermis excised	8.67	2.52	9.89	4.26	–0.48	0.662
	Intermediate zone of the cerebellum excised	9.8	4.02	8.5	3.54	0.44	0.661
	Accompanying changes	10	–	9.55	4.01	0.11	1
	Gliosis	9	2.65	9.78	4.27	–0.31	0.789
	Foramen of Luschka extended	11.43	3.1	7	3.39	1.98	0.048
	DTI asymmetry	11.6	4.16	8.14	3.08	1.54	0.146

	DTI asymmetry: site with more volume	9.33	1.53	7.25	3.86	0.89	0.527
	Cerebellum symmetry	8.14	3.08	11.6	4.16	–1.54	0.139
Bricks patterns	Vermis excised	7.67	6.11	8.67	3.77	–0.36	0.778
	Part of vermis excised	7.67	6.11	8.8	3.11	0.36	0.944
	Upper part of vermis excised	8.38	4.07	8.5	5	–0.05	1
	Middle part of vermis excised	11	2	7.56	4.42	1.24	0.287
	Lower part of vermis excised	8.67	3.51	8.33	4.56	0.12	0.94
	Intermediate zone of the cerebellum excised	8.7	4.45	7	2.83	0.53	0.757
	Accompanying changes	11	–	8.18	4.29	0.65	0.752
	Gliosis	9	3.46	8.22	4.55	0.28	0.845
	Foramen of Luschka extended	10.14	2.19	6	5.29	1.7	0.1
	DTI asymmetry	9.6	2.97	7.57	4.89	0.83	0.448

	DTI asymmetry: site with more volume	9.67	3.21	6	5.77	0.98	0.344
	Cerebellum symmetry	7.57	4.89	9.6	2.97	–0.83	0.462
Puzzles	Vermis excised	10	2.65	10.89	2.8	–0.5	0.708
	Part of vermis excised	10	2.65	10.4	2.61	0.76	0.765
	Upper part of vermis excised	10.25	2.43	11.5	3.32	–0.76	0.512
	Middle part of vermis excised	11.33	2.08	10.44	2.92	0.5	0.717
	Lower part of vermis excised	9	3	11.22	2.49	–1.25	0.277
	Intermediate zone of the cerebellum excised	11.3	2.36	7.5	2.12	1.83	0.111
	Accompanying changes	8	–	10.91	2.66	–1.04	0.33
	Gliosis	8.67	3.06	11.33	2.35	–1.5	0.183
	Foramen of Luschka extended	10.71	1.8	10.6	3.85	0.07	1
	DTI asymmetry	9.6	2.88	11.43	2.44	–1.17	0.29

	DTI asymmetry: site with more volume	12.67	3.06	10.5	1.73	1.16	0.371
	Cerebellum symmetry	11.43	2.44	9.6	2.88	1.17	0.296
Coding	Vermis excised	7.67	6.11	7.44	4.33	0.07	1
	Part of vermis excised	7.67	6.11	7.6	4.62	0.14	0.996
	Upper part of vermis excised	7.63	4.78	7.25	4.65	0.14	0.949
	Middle part of vermis excised	12	2.65	6	4.03	1.99	0.064
	Lower part of vermis excised	9.33	4.04	6.89	4.73	0.81	0.481
	Intermediate zone of the cerebellum excised	7.2	4.57	9	5.66	–0.51	0.683
	Accompanying changes	4	–	7.82	4.6	–0.81	0.579
	Gliosis	7.67	5.51	7.44	4.53	0.07	1
	Foramen of Luschka extended	8.86	4.74	5.6	3.85	1.23	0.258
	DTI asymmetry	7.6	3.58	7.43	5.38	0.06	1

	DTI asymmetry: site with more volume	7	4.36	7.75	6.7	–0.18	0.942
	Cerebellum symmetry	7.43	5.38	7.6	3.58	–0.06	1
Age at evaluation	Vermis excised	20.5	7.78	15.78	6.83	0.88	0.46
	Part of vermis excised	20.5	7.78	16.6	6.58	0.88	0.691
	Upper part of vermis excised	17.71	6.52	14.75	8.02	0.69	0.52
	Middle part of vermis excised	25.5	0.71	14.67	5.89	2.02	0.053
	Lower part of vermis excised	20.33	6.03	15.25	6.98	1.09	0.299
	Intermediate zone of the cerebellum excised	15.11	6.55	23.5	3.54	–1.56	0.131
	Accompanying changes	10	–	17.3	6.85	–1.01	0.546
	Gliosis	18.67	7.77	15.88	6.9	0.6	0.593
	Foramen of Luschka extended	18.17	8.18	14.8	5.12	0.81	0.447
	DTI asymmetry	16.25	8.66	16.86	6.39	–0.14	0.913

	DTI asymmetry: site with more volume	15.33	1.53	18	8.72	–0.55	0.625
	Cerebellum symmetry	16.86	6.39	16.25	8.66	0.14	0.903
Age of diagnosis	Vermis excised	13	3.77	8.56	5.02	1.34	0.197
	Part of vermis excised	13	3.77	8.6	5.24	1.34	0.408
	Upper part of vermis excised	10.25	4.99	8.5	5.52	0.57	0.578
	Middle part of vermis excised	15.5	2.6	7.72	3.95	2.34	0.01
	Lower part of vermis excised	10.33	6.29	9.44	4.91	0.27	0.795
	Intermediate zone of the cerebellum excised	8.95	4.89	13.25	5.3	–1.11	0.31
	Accompanying changes	7.5	–	9.86	5.19	–0.45	0.756
	Gliosis	11.33	5.01	9.11	5.16	0.67	0.54
	Foramen of Luschka extended	11.79	5.33	6.7	2.66	1.74	0.091
	DTI asymmetry	10.1	4.94	9.36	5.4	0.25	0.834

	DTI asymmetry: site with more volume	6.17	1.76	11.75	6.2	–1.35	0.26
	Cerebellum symmetry	9.36	5.4	10.1	4.94	–0.25	0.841
End of treatment	Vermis excised	14.5	4.27	10.11	4.91	1.32	0.219
	Part of vermis excised	14.5	4.27	10.3	5.06	1.32	0.424
	Upper part of vermis excised	11.88	4.96	9.88	5.48	0.66	0.514
	Middle part of vermis excised	17.17	2.75	9.22	3.8	2.39	0.01
	Lower part of vermis excised	12.33	6.11	10.83	4.91	0.45	0.651
	Intermediate zone of the cerebellum excised	10.45	4.79	15	5.66	–1.18	0.207
	Accompanying changes	10	–	11.32	5.21	–0.25	0.832
	Gliosis	13.17	4.65	10.56	5.17	0.79	0.465
	Foramen of Luschka extended	13.43	5.22	8.1	2.56	1.83	0.066
	DTI asymmetry	11.9	5	10.71	5.3	0.41	0.719

	DTI asymmetry: site with more volume	7.83	1.44	12.88	6.34	–1.25	0.314
	Cerebellum symmetry	10.71	5.3	11.9	5	–0.41	0.712
Age at the beginning of the treatment	Vermis excised	21	5.57	16.56	7.28	0.96	0.386
	Part of vermis excised	21	5.57	17.4	6.88	0.96	0.631
	Upper part of vermis excised	18.75	6.27	15.5	8.7	0.76	0.482
	Middle part of vermis excised	24.33	2.08	15.44	6.56	1.92	0.068
	Lower part of vermis excised	21	6.24	16.56	7.14	0.96	0.388
	Intermediate zone of the cerebellum excised	16.3	6.78	24.5	2.12	–1.52	0.155
	Accompanying changes	11	–	18.27	6.94	–1	0.497
	Gliosis	19.67	7.57	17	7.07	0.58	0.606
	Foramen of Luschka extended	19.43	7.59	15.2	5.76	1.04	0.324
	DTI asymmetry	18	7.97	17.43	6.78	0.14	0.894

	DTI asymmetry: site with more volume	16	1.73	18.5	9.29	–0.48	0.712
	Cerebellum symmetry	17.43	6.78	18	7.97	–0.14	0.9
Treatment time	Vermis excised	6.5	1.8	6.44	3.86	0.02	1
	Part of vermis excised	6.5	1.8	7.1	3.38	0.6	0.835
	Upper part of vermis excised	6.88	2.75	5.63	4.78	0.6	0.565
	Middle part of vermis excised	7.17	0.76	6.22	3.91	0.42	0.702
	Lower part of vermis excised	8.67	2.89	5.72	3.35	1.31	0.227
	Intermediate zone of the cerebellum excised	5.85	3.18	9.5	3.54	–1.39	0.185
	Accompanying changes	1	——	6.95	3.05	–1.69	0.17
	Gliosis	6.5	5.5	6.44	2.86	0.02	1
	Foramen of Luschka extended	6	3.08	7.1	4.04	–0.56	0.624
	DTI asymmetry	6.1	4.42	6.71	2.78	–0.31	0.778

	DTI asymmetry: site with more volume	8.17	1.61	5.63	3.17	1.2	0.233
	Cerebellum symmetry	6.71	2.78	6.1	4.42	0.31	0.766

*for DTI asymmetry: site with more volume No = L, Yes = R