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NEUROPSYCHOLOGICAL FUNCTIONING OF CHILDREN WITH BRAIN TUMORS

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SUMMARY – In the past few decades, the survivor rate from childhood cancers has significantly increased due to constant modifications and improvements in treatment protocols, so the estimates are that childhood cancer occurs in 1 *per* 600 children, and that 1 *per* 450 adolescents or young adults is a long-term cancer survivor. Nevertheless, radiation treatment is still a necessary option that certainly contributes to greater survival rate (75%), until new approaches to patients with malignant diseases are accepted. In our clinical practice, surgical treatment for malignant brain tumor is followed by radio- and chemotherapy tailored according to patient age and tumor type, position and size. During a six-year period, neuropsychological functioning was tested in 21 patients upon completion of treatment and retested in 19 patients in the stage of primary disease remission. Comparison of the test-retest results revealed some, statistically nonsignificant decline in full scale IQ, verbal and performance subscales, and graphomotor skills. However, the results showed a statistically significant improvement in several cognitive functions including short-term memory, information fund (suggesting long-term memory improvement), visuospatial functions measured by object assemble and block design subtests. There were no statistically significant differences between the patients younger and older than 7 years. Results also suggested an improved quality of recovery expressed by numerous school re-entries, without age or sex differences. Trials are continued to follow-up the possible long-term adverse effects of the aggressive oncologic therapy.

Key words: *Cognitive Disorders – Etiology; Brain Neoplasms – Therapy; Neuropsychology – Adverse Effects*

Introduction

Neuropsychological follow-up of children with malignant diseases is focused on recording and assessment of neurobehavioral toxicity associated with complex oncologic therapy. Unfortunately, most of the neuropsychological testing, including ours, is conducted in the period after surgical treatment followed by aggressive oncologic therapy, so there is no baseline information on the patient cognition before therapy introduction[1,2]. During and after therapy completion, various effects are observed, from endocrine toxicity and associated problems in development, growth and reproductive capabilities, to secondary brain tumors and neurocognitive deficits, where change in IQ scores is the most frequently reported effect, more severe in younger children. In the past few decades, therapy protocols have mostly being corrected and the survival rates have increased, yet even the latest studies support an inverse relation between the age at the time of treatment and later IQ scores. Patients under 7 years of age demonstrated greater cognitive deficits than their older counterparts[3-6]. As no such effects were observed in the first year of treatment initiation, cognitive lesions were presumed to progressively worsen with time. However, radiation therapy remains especially efficacious in the management of malignant brain tumors in childhood and the increased 5-year survival rates of childhood cancers from 55.9% in 1974-1976 to 78.6% in 1995-2001 are considered to be attributable to this mode of treatment[7].

In order to get an insight into the neuropsychological functioning of our patients upon completion of treatment, during a six-year period we performed neuropsychological testing of a wide range of functions to identi-

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fy possible dysfunctions as cognitive lesions due to the administration of aggressive oncologic therapy. The same patients underwent retesting to establish the extension and direction of changes in the neuropsychological functions tested during the period of prolonged remission. Upon completion of the initial aggressive therapy, we observed successful global physical recovery, while still being concerned about the possible neuropsychological outcomes.

Patients and Methods

During the period from January 2002 to December 2007, we collected results of neuropsychological testing of 21 patients with malignant brain tumors treated at Department of Hematology and Oncology, University Department of Pediatrics. The patients were aged 3 to 16 years. There were 11 preschool children aged 3 to 7 years, and ten schoolchildren aged 7 to 16 years. There were nine girls and 12 boys.

After the preliminary diagnosis had been established, the patients underwent neurosurgical procedure. Depending on the histopathologic diagnosis, tumor extensiveness and patient age, the treatment was continued using combined chemo- and radiotherapy according to the GOPH-HIT-MED'99; HIT-SKK'99 protocol[8,9].

Study patients were first tested upon therapy completion. Nineteen patients underwent retesting at 1-3 years of the initial testing. Records of the test-retest results enabled appropriate statistical processing.

Preschool children were tested using preschool development scales RTČ[10] and SPP-3[11] that include measures of full-scale IQ (FSIQ, comparable to Stanford-Binet Intelligence Scale for Children); and GTPO test[12,13] for graphomotor skills, with results in percentiles related to age.

Schoolchildren were tested with REVISK test[14] comparable to HAWIK-R test[15], also including measures of FSIQ, consisting of two subscales – verbal IQ and performance IQ, each subscale subsuming specific subtests: 6 verbal and 5 performance tests. Verbal subtests: information fund, numeric reasoning, reasoning by experience, vocabulary, linguistic generalization, and short-term memory span. Performance subtests: visual perception, object assemble, block design, perceptive-motor speed, and strip design. Graphomotor skills were tested with Bender-Göttingen test[13,16] and results presented in percentiles according to age standards.

Data analysis included descriptive statistics (frequencies, means, cross-tabs), paired *t*-test for repeated measures design, and ANOVA one-way analysis of variance[17].

Results

REVISK test-retest results of each patient, 11 functions measured by 11 subtests, were compared in pairs, first *versus* second testing: Pair 1 – information fund, Pair 2 – visual perception, Pair 3 – numeric reasoning, Pair 4 – object assemble, Pair 5 – reasoning by experience, Pair 6 – block design, Pair 7 – vocabulary, Pair 8 – perceptive-motor speed, Pair 9 – linguistic generalization, Pair 10 – strip design, and Pair 11 – short-term memory. Also the global IQ measures for each patient were compared: Pair 12 – full scale IQ, Pair 13 – verbal IQ, and Pair 14 – performance IQ. Finally, the test-retest results in graphomotor Bender test for each patient were compared: Pair 15 – percentiles.

In terms of global measures of neurocognitive functioning, the results of test-retest comparison showed lower FSIQ (average decline by 6.3 points), verbal IQ (average decline by 8.2 points), performance IQ (average decline by 4.0 points) and Bender percentiles on second testing (average decline by 4.1 percentiles), however, differences were not statistically significant ($p<0.05$).

In terms of specific neurocognitive functions measured by the 11 subtests described above, all results recorded on second testing outreached the former ones and in four subtests were statistically significantly better. These four subtests were: information fund ($p<0.007$), object assemble ($p<0.02$), block design ($p<0.01$) and short-term memory span ($p<0.01$), suggesting an improvement in the functions of long-term memory processes, visuospatial reasoning and working (short-term) memory (Table 1).

In our sample, we compared results of 11 children that were diagnosed, treated and first tested at age 3-7 years (younger) and those of 10 children that were diagnosed, treated and tested at age 7-16 years (older). The two groups were compared by the main sign of successful recovery, i.e. coming back or starting attending school. A great majority of children in both groups and of both sexes continued to attend school (Table 2).

The two groups of younger and older patients were also compared with age-matched control groups with the mean IQ of 100, in order to identify the average decline

Table 1. REVISK and Bender test-retest results (Pair 1 – information fund, Pair 2 – visual perception, Pair 3 – numeric reasoning, Pair 4 – object assemble, Pair 5 – reasoning by experience, Pair 6 – block design, Pair 7 – vocabulary, Pair 8 – perceptive-motor speed, Pair 9 – linguistic generalization, Pair 10 – strip design, Pair 11 – short-term memory, Pair 12 – full scale IQ, Pair 13 – verbal IQ, Pair 14 – performance IQ, and Pair 15 – graphomotor Bender test)

	Paired differences					t	df	Sig. (2-tailed)
	Mean	Std. deviation	Std. error Mean	95% Confidence interval of difference Lower	Upper			
Pair 1 **inf1 - inf2**	-3.875	2.900	1.025	-6.300	-1.450	-3.779	7	**.007**
Pair 2 viz1 - viz2	-.125	2.031	.718	-1.823	1.573	-.174	7	.867
Pair 3 num1 - num2	-1.125	1.642	.581	-2.498	.248	-1.938	7	.094
Pair 4 **obj 1 – obj 2**	-4.750	4.683	1.656	-8.665	-.835	-2.869	7	**.024**
Pair 5 shv1 - shv2	-1.125	2.588	.915	-3.288	1.038	-1.230	7	.259
Pair 6 **blo1 – blo 2**	-7.625	6.865	2.427	-13.364	-1.886	-3.142	7	**.016**
Pair 7 voc1- voc 2	-5.143	6.309	2.385	-10.978	.692	-2.157	6	.074
Pair 8 per 1 – per 2	-9.000	11.563	4.088	-18.667	.667	-2.201	7	.064
Pair 9 lin 1 – lin 2	-4.000	2.944	1.472	-8.684	.684	-2.717	3	.073
Pair 10 str1 - str2	-.250	1.500	.750	-2.637	2.137	-.333	3	.761
Pair 11 **mem1-mem2**	-2.125	1.727	.611	-3.569	-.681	-3.480	7	**.010**
Pair 12 FSQ1 - FSQ2	6.375	14.292	3.573	-1.240	13.990	1.784	15	.095
Pair 13 verIQ1 – verIQ2	8.286	15.804	4.224	-.839	17.411	1.962	13	.072
Pair 14 perIQ1 - perIQ2	4.000	11.688	3.524	-3.852	11.852	1.135	10	.283
Pair 15 Ben1 - Ben2	4.1857	27.0623	7.2327	-11.4396	19.8110	.579	13	.573

and within-group variations (Table 3). The results showed the mean FSIQ to have decreased on retesting by 8.6 and 2 points; the mean verbal IQ by 10.5 and 2.6 points; and the mean performance IQ by only 2.9 and 8 points in younger and older children, respectively. On retesting, the mean results in graphomotor skills were by 3.2 percentiles lower in younger children and by 1.5 percentiles higher in older children.

ANOVA analysis yielded no statistically significant differences in the test-retest results on the measures of FSIQ, verbal IQ, performance IQ and Bender results between the groups of children aged <7 and >7 years (Table 4).

Table 2. Number of children of both sexes attending school after treatment; disease onset and treatment initiation before or after 7 years of age

Sex			Before/after		Total
			Before age 7	After age 7	
Male		Attend school	8	2	10
		School at home	0	1	1
	Total		9	3	12
		No school prog.	1	0	1
Female		Attend school	2	6	8
		No school prog.	0	1	1
	Total		2	7	9

		N	Mean	Std. deviation	Std. error	95% Confidence interval for mean		Minimum	Maximum
						Lower limit	Upper limit		
FSIQ1	younger than 7	11	87.64	17.750	5.352	75.71	99.56	62	114
	older than 7	6	89.50	15.450	6.307	73.29	105.71	67	108
Total		17	88.29	16.503	4.003	79.81	96.78	62	114
FSIQ2	younger than 7	10	79.00	23.395	7.398	62.26	95.74	35	114
	older than 7	8	87.50	19.479	6.887	71.22	103.78	62	112
	Total	18	82.78	21.561	5.082	72.06	93.50	35	114
verIQ1	younger than 7	11	94.82	12.584	3.794	86.36	103.27	76	114
	older than 7	5	95.20	15.659	7.003	75.76	114.64	71	111
	Total	16	94.94	13.077	3.269	87.97	101.91	71	114
verIQ2	younger than 7	9	84.33	24.151	8.050	65.77	102.90	40	118
	older than 7	8	92.63	18.570	6.565	77.10	108.15	65	114
	Total	17	88.24	21.464	5.206	77.20	99.27	40	118
nevIQ1	younger than 7	3	82.33	23.714	13.691	23.43	141.24	56	102
	older than 7	9	93.22	17.188	5.729	80.01	106.43	60	109
	Total	12	90.50	18.476	5.334	78.76	102.24	56	109
nevIQ2	younger than 7	7	79.43	20.509	7.752	60.46	98.40	55	110
	older than 7	9	85.22	21.885	7.295	68.40	102.04	55	112
	Total	16	82.69	20.797	5.199	71.61	93.77	55	112
Ben1	younger than 7g	9	79.222	15.5787	5.1929	67.247	91.197	49.0	95.0
	older than 7	8	57.450	27.5728	9.7484	34.399	80.501	25.0	98.0
	Total	17	68.976	24.0715	5.8382	56.600	81.353	25.0	98.0
Ben2	younger than 7	8	76.025	33.9688	12.0098	47.626	104.424	11.5	96.0
	older than 7	8	58.925	27.3340	9.6640	36.073	81.777	30.4	98.0
	Total	16	67.475	31.0664	7.7666	50.921	84.029	11.5	98.0

Table 3. Test (1) and retest (2) results in two groups of patients (younger and older than 7 years) in the measures of FSIQ, verbal IQ, performance IQ, and Bender results in percentiles, mean comparable to age controls (minimum and maximum)

Discussion

Cognitive skills mostly affected by central nervous system radiotherapy are memory, attention, fine motor speed and coordination, and mathematic skills, yet no specific set of neuropsychological impairment has been identified. Even more, the location of the tumor may be less important for the prognosis of neuropsychological outcome than other factors such as total radiation quantity or number of modalities used in the treatment. Some studies found no evident changes in FSIQ in the first year of follow up, and some less significant changes were observed after two years[18,19].

A follow up study in breast cancer patients treated with adjuvant chemotherapy compared with patients treated after surgery with radiotherapy alone showed a higher risk of cognitive deficit in patients with adjuvant chemotherapy on the first assessment, but four years of the completion of treatment it was no longer possible to demonstrate any differences in cognitive functioning between the two groups, suggesting that neurocognitive dysfunction following adjuvant chemotherapy was probably transient and improvement may have been expected within a 4-year period[20].

However, there are fewer longitudinal studies that provide evidence for the ongoing slower deterioration 10 years after the completion of radiotherapy, with final IQ score depending on the age of the child at the time of treatment[21], or with problems recorded in cognitive, motor, visual and psychological/emotional functioning 16 years following the diagnosis[22].

While Packer *et al*. did not identify the relation between the radiation dose and late IQ changes[5], Silber *et al*. retrospectively analyzed results of 48 children from two studies diagnosed with acute lymphocytic leukemia and primitive neural ectodermal tumors, periodically tested for IQ that received whole-brain irradiation in various doses (18 Gy, 24 Gy, 22-24 Gy and 32-40 Gy). The results showed no statistically significant difference between patients with different diagnoses, but revealed a predictable final IQ score based on the initial IQ score, dose of irradiation, and age at the time of irradiation. The predicted IQ decline was by 11.9 points less in a 10-year-old patient than in a 3-year-old patient with the same dose of irradiation[23].

Ris and Noll suggest that comprehensive batteries are needed to steer assessment away from IQ scores, so the survey should include more specific neuropsychological functions by which the current effects of brain tumors and treatment could be measured, along with developmental neuropsychological models taking in consideration changes that occur with time[24].

Adult survivors of childhood cancer undergoing a retrospective analysis show a high overall disease burden[25]. Besides cardiopulmonary (cardiac and pulmonary toxicity), endocrine (growth, thyroid dysfunction, gonadal dysfunction, fertility, obesity), late effects of childhood cancer and treatment include neurocognitive effects: children irradiated with 2400-cGy CRT when younger than 7 years lose an average of 13-14 points on FSIQ; deficits in short-term (or working) memory and focused attention result in decreased ability to learn new things; with longer follow up, survivors fall further behind their peers; specific deficits have been shown on tests of fine motor functioning, visual-spatial functioning, nonverbal memory, and attention and concentration; expressive language skills and verbal learning are largely unaffected; academically, children most often have difficulties with mathematics; difficulties with reading and spelling are less frequent[26,27].

Comparison of children undergoing surgery and combined radiotherapy-chemotherapy for cerebellar medulloblastoma with their cousins and siblings by assessing

Table 4. Differences between two age groups (younger and older than 7 years) in FS IQ, verbal IQ, performance IQ and Bender results on first (1) and second (2) testing

Sum of squares		df	Mean square	F	Sig.	
FSIQ1	Between groups	13.484	1	13.484	.047	.832
	Within groups	4344.045	15	289.603		
	Total	4357.529	16			
FSIQ2	Between groups	321.111	1	321.111	.678	.423
	Within groups	7582.000	16	473.875		
	Total	7903.111	17			
VerIQ1	Between groups	.501	1	.501	.003	.959
	Within groups	2564.436	14	183.174		
	Total	2564.938	15			
VerIQ2	Between groups	291.184	1	291.184	.617	.444
	Within groups	7079.875	15	471.992		
	Total	7371.059	16			
NevIQ	Between groups	266.778	1	266.778	.765	.402
	Within groups	3488.222	10	348.822		
	Total	3755.000	11			
NevIQ	Between groups	132.168	1	132.168	.291	.598
	Within groups	6355.270	14	453.948		
	Total	6487.438	15			
Ben1	Between groups	2007.655	1	2007.655	4.146	.060
	Within groups	7263.356	15	484.224		
	Total	9271.011	16			
Ben2	Between groups	1169.640	1	1169.640	1.231	.286
	Within groups	13307.190	14	950.514		
	Total	14476.830	15			

intelligence, executive function, attention, visual perception and short-term memory showed worse performance in all tests. In the group older than 10 years the results were significantly worse only in short-term memory, and in the group younger than 10 years and receiving intrathecal methotrexate the results were significantly worse in all tests[28].

In the search for long-term neurological and neurosensory sequels in adult survivors of childhood brain tumor, the estimates from a large-sample study of patients diagnosed with primary central nervous system tumor showed that 17% of patients developed neurosensory impairment – hearing impairments, legal blindness on one or both eyes, cataracts, double vision; seizure disorders in 25% of patients, including 6.5% of those with the late first occurrence; radiation dose of 30 kGy or more to any cortical segment of the brain was associated with a two-fold risk of a late seizure disorder[29].

Evaluating cognitive deficits in the treatment of early childhood medulloblastoma by postoperative chemotherapy alone, conclusion is that chemotherapy alone is a promising treatment for medulloblastoma in young children without metastases. These patients showed a significantly lower mean IQ than healthy controls, but higher than patients that had received radiotherapy[30].

Our earlier study of children treated for acute lymphoblastic leukemia showed an increased risk of late neurological effects when patients were treated with radiotherapy; even the children treated with smaller doses of radiation had worse results than the children treated with chemotherapy alone. Two decades ago, the radiation doses to the central nervous system used in the treatment of patients with hemoblastoses were much higher than those currently applied, and the indications for this mode of treatment were much broader[31-34].

Our present results do confirm the inverse relation: the lower the age at onset, the greater the decline in FSIQ[4-6], verbal and performance IQ. However, there was no statistically significant difference between the two groups (younger and older than 7 years at diagnosis and treatment initiation) in the results of the initial testing and retesting after 1 to 3 years (Tables 3 and 4).

In the last few years, it has been demonstrated that a moderate dose of radiation using sophisticated techniques does not induce cognitive injury in brain tumor patients. Patients with low-grade brain tumor are capable to regain normal cognitive function after receiving radiotherapy that reduces tumor size. In a 5-year period, improvement was recorded in immediate verbal memory, learning, long-term verbal memory, cognitive flexibility and spatial problem solving[35].

This evidence refers to adult patients, where the pretumor level implies a more or less completed cognitive development, whereas in pediatric patients the development of cognitive functions continues after having been disturbed by the tumor.

According to our results, after the initial surgical treatment followed by oncologic treatment with chemo- and radiotherapy, the development is going on with promising results. In our group of patients, the improvement in intellectual functions showed a statistically significant progress in the functions of short-term and long-term memory, and visuospatial reasoning (Table 1), while the global cognitive status, its verbal and performance aspect, showed slower than expected rate of development as compared to age-adjusted standards (Table 3). However, the measured declines were not as significant as reported elsewhere[13,16,17,28,30].

So, although the global cognitive progress of children with brain tumors continues at a somewhat slower rate, the specific intellectual functions crucial for the process of learning and memorizing appear to develop at a faster rate than expected, suggesting that specific accommodation and adaptation in their further growth and maturation take place in the process of rehabilitation.

It seems that the children cancer survivors develop specific patterns of neuropsychological growth by which they compensate for the cognitive sequels of the disease/treatment; the more so, in some aspects they can even outrun their peers, as reported by some authors[36].

Our analysis showed that there were no statistically significant differences in the test-retest results in FSIQ, verbal IQ, performance IQ and graphomotor skills between the children younger and older than 7 years (Table 4). Other recent studies also report no severe difficulties in psychological outcomes as before: "… studies that have used rigorous, controlled designs, multiple information sources, and standardised measures of social functioning, emotional well-being, and behavioural functioning have not found the same evidence of difficulties that had been reported previously"[37].

Among the findings of the Childhood Cancer Survivor Study, there is evidence of higher global distress and depression scores in the group of childhood cancer survivors than in the control group of siblings, but both groups reflect the ratio found in the general population. Furthermore, no diagnostic or treatment-related variables were directly and significantly associated with in-

creases in distress symptoms in survivors of childhood brain cancer[38]. Our study supports these findings, showing better quality of life in the children after treatment that facilitated their return to school (Table 2). Even more, since the beginning of 2007, the children have an opportunity to attend school during treatment at our hospital, popularly called "school in pajamas"; several teachers from the nearest local school come daily to our patients, thus enabling them to catch up with their peers, learning all the subjects as if being at school, getting grades, and making them easier to take final exams, also making sure that contacts with the original class are maintained. We intend to continue the follow up, to get a more exact insight in the neuropsychological functioning of a larger number of patients over a longer period of time.

Our future expectations rely on new methods and research findings, being always focused on improvement of the recovery process for pediatric oncology patients.

Several new approaches seem promising, such as 3-dimensional radiation by linear accelerator, so to treat a strictly limited area of brain tissue; first evaluations at 5 years of treatment show that children maintain cognitive functioning and patterns of normal development[39].

There is continuous research in psychopharmacology aiming to help decrease cognitive symptoms and improve mood and quality of life. Note should be made of the significant improvement of cognitive symptoms observed in pediatric brain cancer patients treated after radiation with donepezil for six months. The initial study has been followed by the ongoing 2-year follow up study in 35 patients aged 8-17[40].

In addition, great expectations refer to new genetic research (genes already found for inherited breast cancer, colon cancer, kidney tumors) and development of novel methods such as "bugging" tumors to put drugs on target (using bacteria to release liposomal drugs within the tumor)[41], or "smart drugs", i.e. agents that target the specific molecular causes of cancer, which may bring revolution in cancer treatment[42,43].

Conclusions

Using more advanced protocols for necessary aggressive oncologic treatment of malignant brain tumors in children has resulted in global physical recovery of patients. However, we were concerned with the possible cognitive effects; therefore we conducted complex neuropsychological testing in 21 patients and retesting in 19 patients during the 6-year period, with the following results.

While the global cognitive status and its verbal and performance aspects showed slower than expected rate of development as compared to age-specific standards, the measured declines did not reach statistical significance. In addition, there were no statistically significant differences in the test-retest results of FSIQ, verbal IQ, performance IQ and graphomotor skills between the children aged <7 and >7 years. Furthermore, a statistically significant progress was observed in the functions of short-term and long-term memory, as well as in the functions of visuospatial reasoning.

These results supported the idea of several compensatory mechanisms in intellectual functioning after surgical and oncologic treatment. Thus, developmental neuropsychological models should be considered which could identify changes over time, also enabling multiple assessments that are critical on outcome evaluation.

In the future, we expect the as yet quite numerous side effects of oncologic therapy to reduce by including less aggressive but more efficient drugs in treatment protocols, using 3-dimensional irradiation of solid tumors, and introducing novel therapeutic modalities that would exclusively target the tumor while sparing healthy tissue.

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Sažetak

NEUROPSIHOLOŠKO FUNKCIONIRANJE DJECE S TUMOROM MOZGA

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U posljednjih nekoliko desetljeća značajno se povećalo preživljavanje djece oboljele od raka zahvaljujući neprekidnim poboljšanjima protokola liječenja. Procjenjuje se da se rak u djetinjstvu javlja u 1 od 600 djece, te da je 1 od 450 adolescenata ili mladih odraslih preživjeli bolesnik liječen od raka u djetinjstvu. Liječenje zračenjem i dalje je neophodna opcija koja zasigurno doprinosi većem postotku preživljavanja (75%) dok ne budu prihvaćeni novi pristupi u liječenju bolesnika sa zloćudnim bolestima. U našoj kliničkoj praksi bolesnici sa zloćudnim tumorom mozga najprije se podvrgavaju neurokirurškom zahvatu, a zatim odgovarajućoj radio- i kemoterapiji, ovisno o dobi djeteta, te vrsti, smještaju i veličini tumora. U šestogodišnjem razdoblju smo nakon provedenog liječenja procjenjivali neuropsihološko funkcioniranje 21 bolesnika, a u daljnjoj fazi remisije osnovne bolesti ponovno testirali njih 19. Usporedba rezultata zabilježenih na prvom i ponovnom testu pokazala je određeno, ali statistički neznačajno odstupanje u globalnom IQ (cjelovite ljestvice), kako u verbalnoj tako i u neverbalnoj podljestvici, kao i u grafomotornoj vještini. Međutim, ponovno testiranje bolesnika pokazalao je i značajna poboljšanja u nekoliko spoznajnih funkcija, tj. u kratkoročnom pamćenju, fondu informacija (ukazujući na poboljšanja dugoročnog pamćenja), kao i u vizuospacijalnim funkcijama mjerenim subtestovima sastavljanja objekata i kocaka. Nisu nađene statistički značajne razlike u rezultatima bolesnika mlađih i starijih od 7 godina. Poboljšana kvaliteta oporavka vidljiva je i po brojnom uspješnom povratku bolesnika na školsku nastavu, bez razlika s obzirom na dob i spol. Ispitivanje se nastavlja kako bi se pratile moguće dugoročne neželjene posljedice primijenjene agresivne onkološke terapije.

Ključne riječi: *Spoznajni poremećaji – etiologija; Novotvorine mozga – terapija; Neuropsihologija – štetni učinci*