Neuropsychological Evaluation of Children With Intracranial Tumors: Impact of Treatment Modalities

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ABSTRACT

Antineoplastic treatment has a deleterious effect on intellectual functions, which is mainly attributable to radiotherapy. With the object of determining the neuropsychological disturbances associated with brain irradiation in the child, and to try to differentiate them from the effects caused by the other types of treatment (surgical and chemotherapy) as well as from the effects of the tumor itself, a cross-sectional study was carried out in 25 survivors of medial edge intracranial tumors. In order to monitor the effect of systemic chemotherapy on the cognitive functions, and the effect of prolonged absence from school, two control groups were formed, one made up of subjects treated with chemotherapy for extracranial tumors, and the other of patients with nonmalignant chronic disease. Neuropsychological functions were measured using the Spanish version of the Wechsler scale, as well as the following tests: Spreen-Benton, ITPA and TALE scales, Yuste Memory Test, Thurstone Attention Test, and the Rey Complex Figure.

In addition to a progressive decline found in the full scale intelligence quotient in children irradiated for intracranial tumors, variance analysis showed that these patients deteriorate mainly in visual attention and memory, but also significantly in verbal fluency and in the Performance Intelligence Quotient and all its subtests, when compared to the control groups. Visual attention and the Wechsler Picture Arrangement and Block Designs, were the tests whose decline correlated with the total radiation administered. The article relates this specific neuropsychological injury with the total brain irradiation dose but also with the structures located in the cone-down fields of irradiation to boost regions in the middle edge intracranial content.

KEY WORDS

Intracranial tumors
Cognitive sequelae
Radiotherapy
Chemotherapy

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INTRODUCTION

At the present time, 1 in every 1,000 adults in the 20-year-old age group is a survivor of childhood cancer [1]. Central nervous system (CNS) tumors take second place after leukemia in the league chart of most frequent malignant conditions suffered in childhood, representing about 20% of these kinds of illnesses suffered in childhood and adolescence [2]. Radiotherapy (RT) is an important treatment modality used for child intracranial tumors (ICT). This treatment requires the delivery of radical irradiation, usually after surgery, and sometimes followed by whole-brain prophylactic irradiation in order to sterilize any possible ICT extension [3]. Post-mortem examinations reveal that the physiopathological changes produced in the CNS by radiation and chemotherapy (CT) have been described as a necrotizing leukoencephalopathy and a mineralizing microangiopathy [4,5]. The increase in life expectancy brought about by the use of megavoltage radiation has enabled the effect on cognitive functions [6-8]. Given that 70% of both supra and infratentorial ICT in children are extrahemispherical [9], the posttreatment effect on functional motor handicaps is minimal, whilst the deleterious effect on neuropsychological abilities is far more significant.

With the aim of evaluating the effect of RT on intellectual functions, several studies have been carried out on children with leukemia treated with CNS irradiation. In this type of condition the deterioration of cognitive functions can only be attributed to the iatrogenic effect of the treatment [10-15]. These studies, however, have one principal drawback: all the patients receive the same total dose (1,800 or 2,400 cGy), which is relatively low compared to that usually used in the treatment of ICT. The aims of the present study on children treated by RT for brain tumors were: a) to verify a deleterious effect on intellectual function produced by RT in these children, attempting to differentiate it from that produced by other types of treatment (surgery and CT) and the tumor itself; and b) to evaluate the possible correlation between the dose of the RT with the degree of neuropsychological deterioration. How this deterioration progresses on time and if the specific intellectual functions affected by the RT vary as a function of the age at which the irradiation is given, has been published separately [16].

MATERIALS AND METHODS

Between 1980 and 1990, 63 children with ICT were seen in the Clínica Universitaria de Navarra (Service of Pediatric Oncology, Service of Child Neurology, and Service of Radiotherapy). All of them were treated with the conventional doses of RT in a radical therapy attempt. Correlatively 25 of them were taken into account for this study on the basis that they satisfied the following criteria: 1) ≤ 15 years old when treated; 2) normal psychomotor development up to the commencement of RT; 3) that in every case the tumor was of middle edge and extra-hemispheric, maintaining the integrity of the cerebral hemispheres insofar as the direct action of the tumor and surgery are concerned; 4) that 6 months had elapsed since treatment, allowing a reasonable time for the patient to recover from the effects of surgery and intracranial hypertension, so that only the neuropsychological sequelae of the treatment (CT, RT) would remain. The types and location of the tumors are set out in Table I.

Two control groups of 25 children each were established (Table II). In order to control the possible effect on cognitive functions produced by CT the first group consisted of patients who had received CT for extracranial tumors (ECT), since some of the patients with ICT had received (CT) in addition to RT. The second group were patients with nonmalignant chronic illness (CHR) in order to control the effects of prolonged absence from school and the emotional disorders caused by serious illness.

The children in these groups were matched with the index group for duration of posttreatment period, age at neuropsychological assessment, and in parental socioeconomic status, graded as (1) primary schooling and low-level employees or manual jobs or (2) secondary/ university degrees and technical/intellectual jobs. The preillness intelligence quotient (IQ) was also similar in the three groups, according to the school intelligence tests carried out before the development of illness. If this information was unavailable, IQ level was estimated by a team of school psychologists on the basis of preillness school grades. The homogeneity of the three groups in the duration of posttreatment period, age at neuropsychological assessment, IQ preillness, and parental sociocultural level was provided statistically (t-test, Mann-Whitney U test, chi-square, and correlation testing).

In order to quantify the different types and doses of the RT received by the children, an RT score was established by a senior radiotherapist for use with statistical analysis. This score was: $\text{cGy of whole-brain RT} + (\text{cGy of in-volved field RT} \times \text{the ratio of the brain volume included in the boost})$. The volume of the geometric figure closest to the brain volume radiated in the boost, according to measures given by X-ray simulation films, divided by whole-brain volume (equivalent to sum of a semisphere plus a semiovoid with the measures given by X-ray simulation films), gave the ratio of the encephalic volume radiated in the boost.

In order to quantify the CT given to the ICT and ECT, a CT score was also established. Since the high doses of methotrexate (MTX) intravenously (i.v.) or the MTX-IT are reported to have a harmful effect on the CNS [4], every 6 g i.v. of MTX or every conventional administration of MTX-IT was quantified as 1 point. And so was considered as 1 point every dose of CT intra-arterial (i.a.) given directly to the brain (CDDP i.a., BCNU i.a., THIO i.a.). Finally, every whole i.v. administration of other CT agents, since they are not reported to be deleterious for the brain, was only quantified as 0.1 point.

The neuropsychological assessment was performed using the full and specific scores of the Spanish version of the Wechsler scale [17], as well as the following (Table III): Spreen-Benton [18], ITPA [19] and TALE scales [20], Yuste Memory Test [21], Thurstone Attention Test [22], and the Rey Complex Figure [23]. The WISC-R was not used because it had not been standardized on Spanish children at the time of our study. Standardized scores were used where available, and direct test scores were not (Table IV). This was possible because the ages of the three groups had been matched.

Statistical analysis (one-way variance and mean homogeneity analysis) was carried out using parametric and nonparametric statistics, according to whether or not the data were distributed in a normal or uniform manner. Distribution of the data was analyzed by a "normality test" (Statworks). A linear regression test was applied to relate the degree of

cognitive deterioration (test scores) to the dose of RT administered (RT score). Significance was set at 5%.

RESULTS

The 25 children with ICT were assessed at time intervals from 6 months to 10 years after treatment. The neuropsychological assessment state of the patient population was as follows: 56% had full scale intelligence quotient (FSIQ) greater than 90; 28% had FSIQ level between 70 and 90; and 16% had FSIQ lower than 70.

Comparing preillness IQ and the IQ at our assessment, the decline in FSIQ level was from a mean of 110.2 to a 92, and the drop was as follows: 23% of the patients experienced a drop of 10 points from their FSIQ score prior to RT; 29.5% dropped between 10- to 20 points; and 23.5% lost more than 30 points from their preradiotherapy FSIQ score. In the other groups the mean IQ pre and postillness were in the ECT 107.07 and 107.04, respectively, and in the CHR 108.1 and 106.92.

The FSIQ deteriorated progressively. Among children assessed less than 3 years after RT 31% showed an FSIQ less than 90 with an average fall of 17.6 points, however, of those assessed at least 3 years after RT, 58% had an FSIQ of less than 90 and an average fall of 22.3 points (Fig. 1).

Table IV records the means and variation values in the three groups of patients for all the tests applied. The statistical analysis among groups, using parametric and nonparametric tests, shows that the ICT patients present statistically significant differences in FSIQ, Performance IQ (PIQ) and all its subtests (Picture Completion, Picture Arrangements, Object Assembly, Coding, and Block Designs), verbal fluency, visual attention, and verbal and visual memory (Tables V and VI).

To investigate the influence of the dose of RT on the severity of the sequelae, we performed two types of analyses. First, a regression analysis was carried out between the standardized scores of the tests and the RT administered (RT score). Significant regression emerged in the Wechsler performance subtest Block Design ($r = 0.45/ P = 0.03$) and in the Visual Attention test ($r = 0.52/ P = 0.01$). Second, we divided the group of children into two subgroups according to whether they had an RT score of less than 3,000 (9 children) or greater than 3,000 (16 children), since some regression-scattergrams showed a drop of the test scores environs an RT score of 3,000. Comparison of the two subgroups revealed significant differences for PIQ, for the Wechsler performance subtests Picture Arrangement and Block Design, and for the Visual Attention test (Table VII).

Therefore, it appears that the degree of deterioration in general cognition (Picture Arrangement, and the parameter "Decline" which approaches significance in Table VII), in attention, and in visual-spatial skills (PIQ, Block Design, and Coding which also approaches significance in Table VII), correlates significantly with the total dose of RT. Since an RT score lower than 3,000 corresponds to involved field radiation without whole-brain RT (Table I), it might be assumed that the addition of whole-brain RT to the conventional doses administered adds a significant risk of greater compromise for the specific intellectual functions which tend to be affected.

DISCUSSION

The radiation doses used in the treatment of ICT induces a neuropsychological deterioration clearly different from that produced by the action of the tumor itself. This deterioration was not seen in children suffering from CHR nor in children with ECT who had received more intense CT (the mean of CT score for the ICT group was 8.7 and for the ICT group 1.1).

There is some controversy of whether or not, when administered together, CT (mainly MTX) and RT potentiate their effect on normal CNS [4,24]. However, given that only 11 of the children with ICT in this study received neurotoxic drugs with radiation, and this CT was in low dose, and having controlled other variables by the research design, the deterioration observed appears to be largely attributable to RT. Hydrocephaly might also contribute to the deterioration observed. However, Ellenberg et al. [25] have suggested that acute hydrocephaly, in contrast to its chronic form, has not been shown to be an important contributing factor in neuropsychological deterioration since its effects are transitory. Once eliminated, attentional function is restored and bradypsychia disappears.

Children who received RT for middle edge cerebral tumors deteriorated most in visual and verbal memory (Yuste Memory Test and Rey Complex Figure Memory Test), that is, in the ability to identify something as meaningful and to process it in such a way that it can later be remembered; in attention capacity and visual discrimination skills (Visual Attention Test and the Wechsler performance subtests Picture Completion and Coding Tests); in verbal fluency (ITPA Verbal Fluency Test) involving agility in verbalized thinking; and in manual praxias (PIQ and its Object Assembly and Block Design subtests), which measure perception of spatial relations, eye-hand coordination, and anticipatory-sequencing-strategy skills. In summary, children who underwent brain irradiation deteriorated in a number of specific cognitive functions: the most affected was memory, followed by attention capacity, verbal fluency, and sequential processing. Duffner et al. [8,26], Kun and Mulhern [27], Packer et al. [28], Bendersky et al. [29], and Morrow et al. [30] have also found selective deficiencies in memory, attention ability, and visual-spatial organizational skills.

The functional circuit to which attentional and memorial abilities refer is composed of the reticular ascending substance and the limbic-mammillo-thalamic-neostriate-orbitomesial connections [31-35]. All these structures are usually located in the cone-down fields of the irradiation to boost regions in the middle-edge of the intracranial content. Moreover, this latter circuit influences the selective activation or inhibition of all the convex areas which are directly affected in most cases by the whole-brain RT [36-38]. A reduction in whole-brain radiation would decrease the damage to the cortical and the subcortical white matter of the convexity (in relation to the intramodal and intermodal associative functions: information-processing tasks), improving the information transmission and associative functions. Perhaps dosages similar to those used in meningeal prophylaxis in children with leukemia would be sufficient to sterilize any possible micrometastases of the ICT. It is controversial whether or not such a reduction would be preferable also from the point of view that these lower dosages produce a less significant deterioration in neuropsychological functions [39,40]. Tomita and Mclone [41], Brand et al. [42], and Halberg et al. [43] have shown that the prophylactic radiation dose to the cranial-spinal axis can be decreased without

jeopardizing control rate and survival in patients, mainly in those low risk patients who have had a total surgical tumor resection and negative myelography and cerebrospinal fluid cytology.

Three-dimensional treatment techniques, and target volumen estimations performed with magnetic resonance imaging (that try to avoid structures related to attentional and memorial functions in the cases where they are not affected by the tumor), will permit more accurate design of treatment programs that will attempt to decrease the long-term sequelae of ICT patients and no compromise of disease control rates.

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Table 1. Data Relating to the Patients, Their Tumors, and the RT Received

Type of tumor	Age at RT (years)	Interval to assessment (months)	Whole-brain RT (cGy)	Involved RT (cGy)	Ratio ^a	Score RT ^b
1. Medulloblastoma (posterior fossa)	12	6	3,000	2,000	0.27	4,396
2. Medulloblastoma (posterior fossa)	6	7	2,600	3,000	0.20	3,768
3. Pons oligodendroglioma (middle fossa)	2	7		5,000	0.51	2,527
4. Astrocytoma IV v. (posterior fossa)	15	7	3,000	2,000	0.15	3,752
5. Thalamic multiform glioma (middle fossa)	12	8	3,000	2,000	0.22	4,075
6. Medulloblastoma (posterior fossa)	14	8	3,000	2,000	0.15	3,751
7. Pineal tumor (middle fossa)	7	14	3,000	2,000	0.13	3,671
8. Optic glioma (anterior fossa)	13	18		6,000	0.65	3,900
9. Ependymoma IV v. (posterior fossa)	15	18	3,000	2,600	0.2	4,099
10. Medulloblastoma (posterior fossa)	14	28	3,000	2,600	0.14	3,771
11. Ependymoma IV v. (posterior fossa)	4	33	3,000	2,000	0.17	3,837
12. Optochiasmatic glioma (anterior/middle fossa)	2	35		5,600	0.42	2,357
13. Optic glioma (anterior fossa)	4	35		5,400	0.17	903
14. Cerebellar astrocytoma (posterior fossa)	9	37		5,800	0.35	2,030
15. Ependymoma IV v. (posterior fossa)	8	38	2,600	2,800	0.24	3,884
16. Ependymoma IV v. (posterior fossa)	2	48	3,000	2,400	0.21	4,108
17. Astrocytoma floor III v. (middle fossa)	9	48		6,000	0.5	3,000
18. Optic glioma (anterior fossa)	2	56		5,000	0.16	800
19. Optic glioma (anterior fossa)	5	60		5,000	0.17	824
20. Medulloblastoma (posterior fossa)	2	74	3,200	1,600	0.15	3,940
21. Optochiasmatic astrocytoma (anterior/middle fossa)	5	77		4,839	0.47	2,278
22. Brain stem glioma (middle fossa)	6	120		9,360	0.7	6,595
23. Medulloblastoma (posterior fossa)	9	120	4,000	1,200	0.11	4,580
24. Medulloblastoma (posterior fossa)	9	120	3,000	2,000	0.18	3,900
25. Cerebellar astrocytoma (posterior fossa)	15	120		4,950	0.37	1,833

^beGy of whole-brain RT + (cGy of involved field RT x the ratio^a of brain volume included in the boost).

Table 2. Diseases in the ECT and CHR Groups	
1. Osteoblastic osteosarcoma (left humerus)	Portal hypertension with bloody esophagic varices
2. Chondroblastic osteosarcoma (right femur)	Crohn's disease
3. Acute lymphoblastic leukemia (no RT given)	Juvenile rheumatoid arthritis (Still's disease)
4. Osteoblastic osteosarcoma (right humerus)	Disseminated lupus erythematosus
5. Osteoblastic osteosarcoma (right femur)	Crohn's disease
6. Osteoblastic osteosarcoma (left tibia)	Juvenile rheumatoid arthritis (Still's disease)
7. Osteoblastic osteosarcoma (right tibia)	Polyarticular rheumatoid arthritis
8. Osteoblastic osteosarcoma (right femur)	Juvenile rheumatoid arthritis (Still's disease)
9. Osteoblastic osteosarcoma (left femur)	Important scoliosis (operated, long immobilization)
10. Osteoblastic osteosarcoma (right tibia)	Juvenile rheumatoid arthritis (Still's disease)
11. Abdominal lymphoblastic lymphoma (T cells)	Mucoviscidosis
12. Cervical lymphoblastic lymphoma (T cells)	Polyarticular rheumatoid arthritis
13. Rhabdomyosarcoma (urinary bladder)	Polyarticular rheumatoid arthritis
14. Osteoblastic osteosarcoma (left femur)	Juvenile rheumatoid arthritis (Still's disease)
15. Ewing sarcoma (left femur)	Turner's syndrome (limbs lengthening)
16. Hodgkin's disease (IV A)	Fallot tetralogy (several endocarditis, pacemaker)
17. Suprarenal neuroblastoma	Mucoviscidosis
18. Ewing sarcoma (left perone)	Polyarticular rheumatoid arthritis
19. Suprarenal neuroblastoma	Polyarticular rheumatoid arthritis
20. Pheochromocytoma	Primary amyloidosis
21. Ewing sarcoma (fifth rib left)	Chronic autoimmune hepatopathy (several biopsies)
22. Ewing sarcoma (left tibia)	Juvenile rheumatoid arthritis (Still's disease)
23. Ewing sarcoma (left tibia)	Chronic granulomatous disease
24. Osteoblastic osteosarcoma (left femur)	Active chronic hepatitis (aggressive evolution)
25. Wilms' tumor	Crohn's disease

Table 3. Neuropsychological Evaluation*

General cognition	FSIQ (WISC) Picture Arrangement (WISC) Arithmetics (WISC) Comprehension (WISC)
Language	VIQ (WISC) Vocabulary (WISC) Articulation (S. Bentón) Sentence Memory (S. Bentón) Verbal Fluency (ITPA) Similarities (WISC) Information (WISC)
Visual spatial skills	PIQ (WISC) Copy Rey Complex Figure Block Designs (WISC) Object Assembly (WISC) Picture Completion (WISC) Coding (WISC) Attention Test (Thurstone)
Memory	Digit Span (WISC) Metnory Test (Yuste) Sequential Visual-Motor Memory (ITPA) Memory Rey Complex Figure
Reading, writing	Arbitrary Writing Errors (TALE) Natural Writing Errors (TALE) Reading Test (TALE)

*This distribution of the tests and subtests permits us to evaluate the different specific functions and construct a neuropsychological profile for each patient.

Table 4. Descriptive Statistics of the Three Groups

	ICT		ECT		CHR	
	Mean	SD	Mean	SD	Mean	SD
1. FSIQ	92.04	22.25	107.04	11.60	106.92	10.26
2. VIQ	97.78	14.74	102.92	11.02	103.08	12.59
3. PIQ	93.48	19.03	110.13	12.41	107.4	10.63
4. Picture Arrangement (WISC)	10	3.22	11.71	2.44	12.42	1.82
5. Arithmetic (WISC)	9.54	3.42	10.75	2.35	11.08	2.69
6. Comprehension (WISC)	9.5	2.43	10.38	2.45	10.72	2.30
7. Vocabulary (WISC)	10.83	2.33	11.13	2.03	11.36	2.23
8. Articulation (S. Bentón) ^a	27.78/30	2.92	28.41/30	1.72	27.96/30	2.25
9. Sentence Memory (S. Bentón) ^a	22.17/26	3.46	23.62/26	2.65	23.92/26	2.91
10. Verbal Fluency (ITPA) ^a	68.35	21.22	86.67	23.12	87.16	24.39
11. Similarities (WISC)	10.52	3.09	11.92	1.98	11.48	2.14
12. Information (WISC)	9.87	2.55	9.96	2.74	9.88	3.02
13. Copy Rey Figure ^b	41.52	19.86	52.01	12.09	51.1	9.55
14. Block Designs (WISC)	10.41	3.17	12.46	3.70	11.76	2.40
15. Object Assembly (WISC)	9.74	3.47	12.83	3.41	11.17	2.12
16. Picture Completion (WISC)	9.11	2.75	10.83	2.06	10.33	2.06
17. Attention Test ^b	38.36	14.78	54.69	10.54	53.55	7.75
18. Coding (WISC)	7.94	4.07	11.17	2.62	11.87	3.15
19. Digit Span (WISC)	9	3.27	10.14	2.63	10.63	2.43
20. Memory Test (Yuste) ^b	37.29	9.85	49.01	8.06	51.92	10.46
21. Sequential Visual-Motor Memory (ITPA) ^a	15.78/26	5.04	18.83/26	4.02	17.4/26	4.66
22. Memory Rey Figure ^b	45.80	14.46	55.66	8.50	54.66	10.08
23. Arbitrary Writing Errors (TALE) ^c	5.32	5.09	5.54	4.21	6.7	4.56
24. Natural Writing Errors (TALE) ^c	3.5	5.31	1.42	1.99	1.7	2.51
25. Reading Test (TALE) ^c	7.32	7.25	6.04	5.54	7.22	6.16

^aDirect results. The denominator following oblique denotes maximum score of the test. For Verbal Fluency direct results are also given (number of words spoken). We could not obtain normalized results because these tests are not standardized for Spanish population for ages of our patients.

^bNormalized results (mean 50 SD10). Other tests are WISC subtests (mean 10 SD3).

^cDirect results (number of errors made).

Table 5. One-Way Variance Analysis Among the Three Groups (Data With Normal Uniform Distribution)

	ANOVA P	ICT vs. ECT F2,72	ICT vs. CHR F2,72	ECT vs. CHR F2,72
FSIQ	0.001	5.752 ^a	5.651 ^a	3.7E-4
VIQ	0.281	0.938	1.019	0.001
PIQ	0.0003	7.895 ^a	5.632 ^a	0.221
Comprehension	0.213	0.748	1.505	0.127
Vocabulary	0.703	0.108	0.353	0.071
Articulation	0.638	0.421	0.035	0.226
Sentence Memory	0.111	1.357	2.004	0.058
Verbal Fluency	0.005	3.692 ^a	4.971 ^a	0.091
Similarities	0.142	1.924	0.926	0.197
Information	0.992	0.006	8.4E-5	0.005
Block Designs	0.077	2.569	1.149	0.306
Picture Completion	0.038	3.241 ^a	1.617	0.285
Memory Test	0.0001	8.894 ^a	14.14 ^a	0.573
Sequential Visual-Motor Memory	0.081	2.602	0.746	0.599

^aStatistical significant differences.**Table 6.** Nonparametric Variance Analysis Among the Three Groups (Data With Neither Normal Nor Uniform Distribution)

	Kruskal-Wallis	U Mann-Whitney		
	P	ICT vs. ECT P	ICT vs. CHR P	ECT vs. CHR P
Picture Arrangement	0.007*	0.032*	0.002*	0.364
Arithmetic	0.129	0.112	0.065	0.613
Copy Rey Figure	0.147	0.063	0.169	0.496
Object Assembly	0.009*	0.004*	0.115	0.059
Attention Test	0.0001*	0.0002*	0.0002.*	0.836
Coding	0.001*	0.003*	0.0008*	0.433
Digit Span	0.260	0.269	0.099	0.721
Memory Rey Figure	0.017*	0.008*	0.022*	0.741
Arbitrary Writing Errors	0.358	0.564	0.147	0.416
Natural Writing Errors	0.093	0.057	0.066	0.735
Reading Test	0.841	0.715	0.918	0.542

*Statistically significant differences.

Table 7. Levels of Statistical Significance Obtained From a Comparison of Test Results of Children Irradiated With a Score of RT Greater and Less Than 3,000

	P	Tests applied
FSIQ	0.2263	t-test
VIQ	0.5312	t-test
PIQ	0.0265*	t-test
Picture Arrangement	0.0373*	U-Mann-Whitney
Arithmetic	0.1349	U-Mann-Whitney
Comprehension	0.3792	t-test
Vocabulary	0.322	t-test
Articulation	0.1706	t-test
Sentence Memory	0.2989	t-test
Verbal Fluency	0.3738	t-test
Similarities	0.1687	t-test
Information	0.8624	t-test
Copy Fey Figure	0.9228	U-Mann-Whitney
Block Design	0.0565*	t-test
Object Assembly	0.1118	U-Mann-Whitney
Picture Completion	0.1077	t-test
Attention Test	0.0201*	U-Mann-Whitney
Coding	0.0802	U-Mann-Whitney
Digit Span	0.7039	U-Mann-Whitney
Memory Test	0.2223	t-test
Sequential Visual-Motor Memory	0.3625	t-test
Memory Rey Figure	0.5849	U-Mann-Whitney
Arbitrary Writing Errors	0.4983	t-test
Natural Writing Errors	0.5309	t-test
Reading Test	0.3974	t-test
FSIQ Decline ^a	0.0834	t-test

* Statistically significant differences.

^a Result obtained by subtracting the preillness and post-RT FSIQ.

Fig. 1. FSIQ deterioration in children irradiated for ICT. Short-term follow-up: 6 months to 3 years post-RT (13 patients), long-term follow-up: 3 years to 10 years post-RT (12 patients). See Table I.

Figure 1. FSIQ deterioration in children irradiated for ICT. Short-term follow-up: 6 months to 3 years post-RT (13 patients), long-term follow-up: 3 years to 10 years post-RT (12 patients). See Table I.