Health-Related Quality of Life and Cognitive Functioning at On- and Off-Treatment Periods in Children Aged between 6-13 Years Old with Brain Tumors: A Prospective Longitudinal Study

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INTRODUCTION

Brain tumors are the second most common form of childhood cancer, and account for approximately 20% of childhood cancer diagnoses.\(^1\) Due to the availability of aggressive combination therapies, including surgical resection, chemotherapy (CT), radiotherapy (RT), and peripheral blood stem cell transplantation, the prognosis for childhood brain tumors has improved considerably over the last several

Purpose: Our study aimed to examine the relationship between intelligence and health-related quality of life (HRQOL) in children (6-13 years old) diagnosed as having a brain tumor. Materials and Methods: We administered a Korean version of the Wechsler Intelligence Scale for Children-III, the Pediatric Quality of Life Inventory, version 4.0 (PedsQL), the Korean version of the Parenting Stress Index-Short Form, and the Korean Version of the Parenting Sense of Competence (K-PSOC) scale before or after initial radiotherapy (T1) and after treatment termination (T2). In total, 13 patients completed both the T1 and T2 interviews. Results: Scores significantly declined between T1 and T2 on the full-scale intelligence quotients (FIQ), verbal intelligence quotients (VIQ), performance intelligence quotients (PIQ), similarity and coding tests, as well as the K-PSOC, which measures parental anxiety. FIQ scores at T1 were correlated with the self-reported PedsQL total scores (r=0.739) and the parent proxy-report PedsQL scores for school functioning (r=0.706) at T2. Also, the FIQ scores at T2 were correlated with the self-reported PedsQL total scores (r=0.748) and scores for physical health (r=0.728) at T2. Conclusion: The cognitive ability and intelligence level of the patients significantly declined between on and off treatment periods, and higher intelligence functioning at both on and off treatment was correlated with long-term higher HRQOL. Further investigations that monitor intelligence, HRQOL and parenting stress over a longer period, using a greater number of participants, are needed.

Key Words: Childhood brain tumors, intelligence, heath-related quality of life, parenting stress, prospective longitudinal study
decades. Approximately 65% of all children treated for brain tumors now achieve long-term survival.

However, due to the location of the tumors, the aggressive nature of the combined therapies, as well as the extended duration of treatment, recovery and rehabilitation periods, children treated for brain tumors are liable to experience long-term difficulties in many areas of their lives, both physically and mentally. Previous research suggests that children successfully treated for brain tumors may have difficulties reintegrating into normal life, maintaining peer relationships, and attaining normal academic milestones, and they are at greater risk of cognitive and mental difficulties compared to children who have been treated for other cancer variants. Parents of children with brain tumors likewise reported high levels of distress, post-traumatic stress, and a lower quality of life. They further reported that their elevated stress level continued for 5 years or more post-diagnosis.

Pediatric health-related quality of life (HRQOL) is multidimensional, consisting at the minimum of physical, psychological (including emotional and cognitive), and social health dimensions, as delineated by the World Health Organization guidelines. HRQOL has emerged as an important health outcome in pediatric cancer clinical trials. Studies addressing the long-term survival of childhood brain tumor patients have reported that such individuals had a lower HRQOL than both their non-diagnosed peers and other childhood cancer survivors.

Intellectual impairment is associated with a younger age at diagnosis, the site and extent of the tumor, the type of surgery, development of infection, increases in intracranial pressure and most significantly the use of RT. Impairment has been shown to significantly impact HRQOL by interfering with academic, vocational, and psycho-social functioning, and is related with the development of significant psychological and behavioral problems. Furthermore, lower intelligence quotients (IQ) seems to be a strong risk factor in poor HRQOL.

Previous cross-sectional studies found that children with brain tumors had a lower HRQOL, and that the parents of children with brain tumors tended to experience stress related to management behavior and temperament of the patient, as well as their parent-child interactions compared to normal controls. However, only a few longitudinal studies examining the links between intelligence, HRQOL, and parenting stress, satisfaction and efficacy have been conducted in Korea.

We, therefore, aimed to compare intelligence, HRQOL, and parenting stress, satisfaction and efficacy in children with brain tumors between on and off treatment periods. We also aimed to examine the relationship between intelligence levels at on and off treatment and HRQOL at off-treatment periods in children with brain tumors. We hypothesized that intelligence would decline from on treatment to off treatment periods, and higher intelligence would be associated with a higher HRQOL. We also anticipated that HRQOL and parenting satisfaction and efficacy would increase, and parenting stress would decrease from on treatment to off treatment.

MATERIALS AND METHODS

Subjects
Between August 2007 and August 2010, 26 newly diagnosed brain tumor patients were enrolled at the Children’s Cancer Unit at the Samsung Medical Center in Seoul, Republic of Korea. After undergoing surgical resection, the patients received two cycles of pre-RT chemotherapy, which consisted of cisplatin, etoposide, vincristine, and cyclophosphamide (cycle A), and carboplatin, etoposide, vincristine, and ifosfamide (cycle B), followed by cranio-spinal radiotherapy (CSRT) with 23.4 Gy and local RT with 30.6 Gy in cases of metastasis (M) of stage 0 or 1 or CSRT 30.6 Gy and local RT with 23.4 Gy in cases of metastasis of stage 2 or 3. After four cycles of post-RT chemotherapy (cycles A, B, A, and B), tandem double high dose chemotherapy with autologous stem cell rescue was performed. Intelligence, HRQOL, and parenting stress, satisfaction and efficacy scores were collected at interviews conducted approximately before or after initial radiotherapy (T1) and again after treatment termination (T2). Fig. 1 is a schematic diagram of the protocol.

In total, 13 patients who completed both T1 and T2 interviews were included in this analysis.

Procedure
We gathered information concerning the patients’ diagnoses, M stage, size of their residual tumor, and whether or not leptomeningeal seeding was present from their medical records.

We administered the Korean version of the Wechsler Intelligence Scale for Children-III (K-WISC-III) in order to assess intelligence; the Pediatric Quality of Life Inventory,
Our study protocol was approved by our institutional review board, and written informed consent was obtained from each enrolled participant or, for minors, the participant’s parents.

Statistical analysis
We analyzed the data using SPSS 17.0 software (version 17.0; SPSS, Chicago, IL, USA) for Windows.

We used the Mann-Whitney test and the Fisher’s exact test to evaluate differences in clinical variables between patients included in the final analysis and patients excluded at T1. We used the Wilcoxon signed-rank test for comparisons of differences in clinical variables between T1 and T2. Spearman’s rank correlation was used to assess relationships between intelligence at T1 and T2 and HRQOL at T2.

The statistical significance level was set at \( p < 0.05 \).

RESULTS

Of the 26 patients who were eligible for study, 5 patients died before T2 assessment, 1 patient withdrew following T1 assessment and 2 patients declined to participate in T2 assessment. Further to this, 5 patients who were under 6 years of age at T1 assessment had to have their intelligence function assessed not by the K-WISC-III but with the Korean version of the Wechsler Preschool and Primary Scales of Intelligence.

They were therefore excluded because of the methodological need for testing to be the same for all participants.

Comparing patients included in the final analysis with those who were not included, except for the 5 patients less than 6 years of age at T1 assessment, there were no significant differences in the mean age at diagnosis of brain tumors, the mean time from definitive diagnosis to T1 assessment, gender ratio, the mean intelligence scores, and mean PedsQL scores (Table 1).

The mean age at diagnosis of brain tumors was 10.15±2.58 years. The mean time from definitive diagnosis to T1 assessment was 3.15±2.15 months, and the mean time from...
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The mean FIQ scores at T1 were correlated with mean self-reported PedsQL total scores \((r=0.739)\) and the mean parent proxy-report PedsQL scores for school functioning \((r=0.706)\) at T2. Also, the mean FIQ scores at T2 were correlated with the mean self-reported PedsQL total scores \((r=0.748)\) and scores for physical health \((r=0.728)\) at T2 (Table 6).

**DISCUSSION**

The present study comprised an early stage investigation of the links between intelligence, HRQOL and parenting stress.

### Table 1. Demographic Characteristics, Intelligence Test Scores and PedsQL Scores between Patients Included in the Final Analysis and Patients Excluded during On-Treatment

|                           | Patients included in the final analysis (n=13), mean (SD) | Patients excluded (n=8), mean (SD) | \(p\) value* |
|---------------------------|----------------------------------------------------------|-----------------------------------|-------------|
| Mean age, yrs             | 10.15 (2.58)                                             | 8.75 (2.55)                       | 0.301       |
| Mean time from definitive diagnosis to T1 assessment, month | 3.15 (2.15)                                             | 3.50 (2.98)                       | 0.860       |
| Gender (%)                |                                                          |                                   | 0.472       |
| Male                      | 8 (61.5)                                                 | 4 (50)                            |             |
| Female                    | 5 (38.5)                                                 | 4 (50)                            |             |
| Mean FIQ                  | 84.62 (12.42)                                            | 85.38 (20.07)                     | 0.972       |
| Mean VIQ                  | 95.58 (12.42)                                            | 95.75 (22.26)                     | 0.804       |
| Information               | 9.85 (2.30)                                              | 9.00 (4.75)                       | 0.804       |
| Similarity                | 10.38 (2.73)                                             | 11.13 (3.72)                      | 0.547       |
| Arithmetic                | 9.85 (3.96)                                              | 8.00 (4.84)                       | 0.414       |
| Vocabulary                | 9.38 (2.22)                                              | 10.75 (3.01)                      | 0.414       |
| Comprehension             | 7.46 (1.76)                                              | 8.00 (2.39)                       | 0.697       |
| Digit span                | 8.62 (2.96)                                              | 9.00 (3.93)                       | 0.697       |
| Mean PIQ                  | 74.92 (17.95)                                            | 75.75 (19.56)                     | 0.804       |
| Picture completion        | 7.92 (2.87)                                              | 9.13 (4.05)                       | 0.645       |
| Coding                    | 5.15 (3.56)                                              | 5.50 (3.81)                       | 0.750       |
| Picture arrangement       | 5.69 (1.97)                                              | 5.75 (2.77)                       | 0.860       |
| Block design              | 7.69 (3.66)                                              | 7.00 (3.96)                       | 0.697       |
| Self-report               |                                                          |                                   |             |
| Total score               | 63.45 (18.81)                                            | 56.23 (19.49)                     | 0.696       |
| Physical health           | 40.00 (31.21)                                            | 40.62 (24.38)                     | 0.829       |
| Emotional functioning     | 80.00 (15.81)                                            | 69.38 (18.41)                     | 0.274       |
| Social functioning        | 84.44 (20.83)                                            | 70.63 (31.68)                     | 0.277       |
| School functioning        | 66.11 (23.29)                                            | 51.25 (27.48)                     | 0.277       |
| Proxy-report              |                                                          |                                   |             |
| Total score               | 56.12 (14.11)                                            | 52.60 (16.24)                     | 0.633       |
| Physical health           | 43.44 (29.48)                                            | 32.83 (26.14)                     | 0.360       |
| Emotional functioning     | 64.50 (25.65)                                            | 70.00 (22.99)                     | 0.633       |
| Social functioning        | 76.00 (15.78)                                            | 71.88 (18.31)                     | 0.573       |
| School functioning        | 48.89 (20.58)                                            | 44.38 (24.27)                     | 0.743       |

PedsQL, Pediatric Quality of Life Inventory, version 4.0; FIQ, full-scale intelligence quotients; VIQ, verbal intelligence quotients; PIQ, performance intelligence quotients.

*Mann-Whitney test or Fisher’s exact test.
Coding scores significantly declined from on treatment to off treatment. Due to risk factors such as age at diagnosis, the site and extent of the tumor, surgery type, infection, and increase in intracranial pressure and the use of radiotherapy, children with brain tumors are at greater risk of declining in intelligence function, especially as demonstrated through performance tasks. These problems have been reported to extend into adulthood in long-term survivors of childhood cancer and can result in poor academic and vocational success, low self-esteem, and behavioral or emotional prob-

### Table 2. Demographic Information and the Disease and Treatment Characteristics of Children with Brain Tumors

| N | Age at Diagnosis, in months | Sex | Tumor type | Tumor site | Surgery | Hydrocephalus | Leptomeningeal seeding | Residual tumor (size >1.5 cm) | Metastasis stage | FIQ | VIQ | PIQ | The duration (month) between T1 and T2 |
|---|-----------------------------|-----|------------|------------|---------|---------------|----------------------|-----------------------------|----------------|-----|-----|-----|-------------------------------------|
| 1 | 161                         | M   | MB         | I          | GTR     | Y             | N                    | N                           | 0              | 85  | 76  | 92  | 85  | 80  | 71  | 15  |
| 2 | 167                         | F   | MB         | I          | GTR     | Y             | N                    | Y                           | 0              | 73  | 71  | 96  | 93  | 50  | 50  | 11  |
| 3 | 140                         | F   | MB         | I          | GTR     | N             | N                    | N                           | 0              | 73  | 72  | 76  | 68  | 77  | 82  | 14  |
| 4 | 132                         | F   | MB         | I          | GTR     | N             | N                    | Y                           | 0              | 76  | 67  | 83  | 68  | 75  | 71  | 13  |
| 5 | 154                         | F   | ATRT       | S          | GTR     | N             | N                    | N                           | 0              | 100 | 103 | 108 | 118 | 91  | 85  | 19  |
| 6 | 90                          | M   | MB         | I          | GTR     | Y             | N                    | N                           | 0              | 99  | 99  | 104 | 105 | 94  | 92  | 15  |
| 7 | 116                         | M   | MB         | I          | STR     | N             | Y                    | Y                           | 3              | 86  | 74  | 89  | 76  | 85  | 78  | 14  |
| 8 | 113                         | M   | MB         | I          | GTR     | Y             | Y                    | N                           | 3              | 85  | 76  | 99  | 89  | 73  | 68  | 12  |
| 9 | 121                         | M   | MB         | I          | GTR     | N             | Y                    | Y                           | 3              | 112 | 104 | 112 | 105 | 108 | 101 | 13  |
| 10| 79                          | M   | ATRT       | S          | GTR     | N             | Y                    | Y                           | 3              | 86  | 79  | 114 | 104 | 55  | 53  | 12  |
| 11| 158                         | F   | MB         | I          | GTR     | N             | N                    | N                           | 0              | 79  | 79  | 89  | 83  | 73  | 79  | 10  |
| 12| 147                         | M   | MB         | S          | STR     | N             | Y                    | Y                           | 2              | 75  | 70  | 105 | 99  | 44  | 43  | 9   |
| 13| 80                          | F   | MB         | S          | STR     | N             | Y                    | N                           | 0              | 71  | 53  | 79  | 67  | 69  | 47  | 8   |

N, number; M, male; F, female; MB, medulloblastoma; ATRT, atypical teratoid rhabdoid tumor; I, infratentorial; S, supratentorial; GTR, gross total resection; STR, subtotal resection; Y, yes; N, no; FIQ, full-scale intelligence quotients; VIQ, verbal intelligence quotients; PIQ, performance intelligence quotients.

0: no evidence of gross subarachnoid hematogenous metastasis, 3: gross nodule seeding in the spinal subarachnoid space, T1: assessment during treatment, T2: assessment after treatment termination.

### Table 3. Comparisons between Intelligence Test Scores during On-Treatment and Off-Treatment Periods in Children with Brain Tumors

| T1 (mean±SD) | T2 (mean±SD) | p value |
|--------------|--------------|---------|
| Mean FIQ     | 84.62 (12.42)| 78.69 (14.88)* | 0.008 |
| Mean VIQ     | 95.58 (12.42)| 89.23 (16.53)* | 0.013 |
| Information  | 9.85 (2.30)  | 8.69 (3.17)   | 0.058 |
| Similarity   | 10.38 (2.73) | 8.31 (2.46)*  | 0.004 |
| Arithmetic   | 9.85 (3.96)  | 9.69 (4.13)   | 0.796 |
| Vocabulary   | 9.38 (2.22)  | 9.08 (2.72)   | 0.578 |
| Comprehension| 7.46 (1.76)  | 6.31 (2.21)   | 0.090 |
| Digit Span   | 8.62 (2.96)  | 7.77 (2.97)   | 0.304 |
| Mean PIQ     | 74.92 (17.95)| 70.77 (18.04)*| 0.041 |
| Picture completion | 7.92 (2.87) | 8.08 (2.90) | 0.751 |
| Coding       | 5.15 (3.56)  | 3.77 (2.39)*  | 0.016 |
| Picture Arrangement | 5.69 (1.97) | 5.77 (3.59) | 0.915 |
| Block Design | 7.69 (3.66)  | 7.23 (3.63)   | 0.386 |

FIQ, full-scale intelligence quotients; VIQ, verbal intelligence quotients; PIQ, performance intelligence quotients; SD, standard deviation.

T1: assessment during treatment, T2: assessment after treatment termination.

*p<0.05, Wilcoxon signed rank test.

satisfaction and efficacy in children diagnosed with brain tumors and their families. We compared intelligence, HRQOL and parenting stress, satisfaction and efficacy between on treatment and off treatment periods, and examined the relationship of intelligence at on and off treatment by assessing HRQOL in the off treatment period.

During on treatment, there were no significant differences in intelligence and HRQOL between patients included and patients excluded.

We found that the mean FIQ, VIQ, PIQ, similarity, and
Table 4. Comparison of the PedsQL Scores of Child Self-Assessment and Parental Proxy-Reporting at On-Treatment and Off-Treatment in Children with Brain Tumors

|                      | T1 (mean±SD) | T2 (mean±SD) | p value | Healthy sample (mean±SD) |
|----------------------|--------------|--------------|---------|--------------------------|
| **Self-report**      |              |              |         |                          |
| Total score          | 63.45 (18.81)| 64.47 (12.81)| 0.612   | 88.16 (10.74)            |
| Physical health      | 40.00 (31.21)| 46.88 (26.24)| 0.352   | 88.44 (12.33)            |
| Emotional functioning| 80.00 (15.81)| 75.00 (13.23)| 0.180   | 82.91 (18.52)            |
| Social functioning   | 84.44 (20.83)| 88.33 (16.00)| 0.465   | 93.55 (11.28)            |
| School functioning   | 66.11 (23.29)| 64.47 (12.81)| 0.833   | 87.22 (13.00)            |
| **Proxy-report**     |              |              |         |                          |
| Total score          | 56.12 (14.11)| 59.16 (14.24)| 0.293   | 90.56 (9.47)             |
| Physical health      | 43.44 (29.48)| 49.32 (21.51)| 0.225   | 92.02 (10.75)            |
| Emotional functioning| 64.50 (25.65)| 71.36 (26.18)| 0.129   | 84.43 (16.40)            |
| Social functioning   | 76.00 (15.78)| 67.32 (24.18)| 0.462   | 94.97 (10.15)            |
| School functioning   | 48.89 (20.58)| 51.50 (13.95)| 0.496   | 89.58 (12.18)            |

PedQL, Pediatric Quality of Life Inventory, version 4.0; SD, standard deviation.
T1: assessment during treatment, T2: assessment after treatment termination.
Healthy sample was derived from Kook and Varni.23
*p<0.05, Wilcoxon signed rank test.

Table 5. Comparisons between the K-PSI-SF and K-PSOC Scores On and Off Treatment in Children with Brain Tumors

|                      | T1 (mean±SD) | T2 (mean±SD) | p value |
|----------------------|--------------|--------------|---------|
| **K-PSI-SF**         |              |              |         |
| Stress related to difficult child | 17.33 (4.64) | 18.60 (2.41) | 0.905   |
| Stress related to parent-child interaction | 24.17 (4.67) | 23.00 (4.22) | 0.231   |
| Stress related to child’s learning | 8.92 (2.75)  | 8.80 (2.44)  | 0.235   |
| **K-PSOC**           |              |              |         |
| Sense of parenting competence | 28.25 (5.36) | 29.00 (3.62) | 0.478   |
| Parental anxiety     | 13.08 (3.42) | 11.40 (3.06)*| 0.027   |

K-PSI-SF, Korean version of the Parenting Stress Index-Short Form; K-PSOC, Korean version of the Parenting Sense of Competence.
T1: assessment during treatment, T2: assessment after treatment termination.
*p<0.05, Wilcoxon signed rank test.

Table 6. Correlation of FIQ, VIQ and PIQ Scores at On- and Off-Treatment with the PedsQL Scores of Child Self-Assessment and Parental Proxy-Reports Off Treatment

|                      | T1                  | T2                  |
|----------------------|---------------------|---------------------|
|                      | FIQ     | VIQ     | PIQ     | FIQ     | VIQ     | PIQ     |
| **Self-report**      |         |         |         |         |         |         |
| Total score          | 0.739*  | 0.395   | 0.450   | 0.748*  | 0.209   | 0.552   |
| Physical health      | 0.594   | 0.368   | 0.285   | 0.728*  | 0.267   | 0.450   |
| Emotional functioning| -0.389  | -0.167  | -0.419  | -0.667  | -0.341  | -0.604  |
| Social functioning   | 0.494   | 0.463   | 0.367   | 0.607   | 0.548   | 0.383   |
| School functioning   | 0.380   | 0.329   | 0.207   | 0.422   | 0.269   | 0.286   |
| **Proxy-report**     |         |         |         |         |         |         |
| Total score          | 0.174   | 0.059   | 0.114   | 0.264   | 0.073   | 0.109   |
| Physical health      | 0.142   | -0.151  | 0.153   | 0.128   | -0.218  | 0.078   |
| Emotional functioning| -0.152  | 0.214   | -0.145  | -0.014  | 0.389   | -0.110  |
| Social functioning   | -0.027  | -0.144  | 0.037   | -0.005  | -0.160  | -0.027  |
| School functioning   | 0.706*  | 0.431   | 0.339   | 0.530   | 0.307   | 0.213   |

FIQ, Full-Scale intelligence quotients; VIQ, verbal intelligence quotients; PIQ, performance intelligence quotients; PedQL, Pediatric Quality of Life Inventory, version 4.0.
T1: assessment during treatment, T2: assessment after treatment termination.
*p<0.05, Spearman correlation analysis.
Many studies on intelligence functioning in children with brain tumors have utilized various Wechsler scales; for subjects younger than 6 years, the primary scale should be used, whereas the children’s scale should be used in children under the age of 16 years, after which the adult scale should be used. Due to scale differences, the comparison of results when using different scales becomes problematic. Our findings showed intelligence declines from on-treatment to off-treatment in brain tumors patients aged 6-16 years, assessed only by K-WISC-III. Reportedly, intellectual functioning declines quickly in the first few years after treatment termination, and then more gradually. Accordingly, longer-term monitoring of intellectual function in children with brain tumors is warranted.

In this study, there were no significant differences found between on-treatment HRQOLs and the off-treatment HRQOLs. However, both the on-treatment HRQOL and the off-treatment HRQOL scores were lower than those observed in a study of Korean healthy children (Table 4), and recent cross-sectional research by our group showed that children with brain tumors had lower HRQOL than a control group. Therefore, we and many other researchers have been interested in the progression of HRQOL levels after brain tumor diagnosis and treatment termination. Previous study results have differed from our findings: one longitudinal study reported significant improvement in HRQOL at 1, 6 and 12 months after diagnosis, but the authors of the aforementioned study did not specify whether the 12 months assessment was performed after termination of the treatment and whether all the individual participants received the same modality of treatment. Moreover, differences in the duration, amount and frequency of RT and CT, subjective responses to the impact of acute side effects, such as nausea, hair loss, and additional hospitalization, levels of individual concern about the long-term consequences of treatment, and trans-cultural and ethnic differences may result in different results in terms of how patients consider their quality of life. For the most successful long-term monitoring of HRQOL after the termination of brain tumor treatment, it is necessary that the studied patients receive the same therapeutic modality.

In this study, there were no significant differences between the level of parental stress at on and off treatment periods, but parental anxiety significantly declined from on treatment to off treatment. Recent cross-sectional research by our group showed that the parents of children with brain tumors tended to experience more parenting stress than the normal control group. Since much of the parental emotional and physical burden (e.g. care-giving, fear of child death, increased sense of helplessness and depression) created by child illness is relieved once the treatment process has completed, it is reasonable to consider that parental anxiety level is also likely to decrease after treatment has concluded. Despite this, even after treatment termination, parents of children with tumors often encounter long-term psychiatric sequelae, neuropsychological dysfunction, and other residual effects of the disease and its treatment, in addition to having an elevated risk of newly rising late effects or further distress created by disease recurrence that requires significant long-term follow-up and care. A significant number of parents still suffer from clinical parenting distress after five years, and as many as 5% to 10% of parents go on to develop post-traumatic stress disorder after their child’s treatment has finished. Thus, careful monitoring of parental stress during off-treatment as well as on-treatment periods in cases of childhood brain tumor is needed.

In this study, decreased general cognitive ability in the on-treatment period was related to lower self-reported HRQOL and parent-rated HRQOL for school functioning in the off-treatment period, and a decreased general cognitive ability in off-treatment periods was related to lower self-reported HRQOL, specifically physical health off-treatment. In previous studies, decreased cognitive ability was associated with low school achievement, low mid-life income and poor physical complaints. Since the prognosis of childhood brain tumors has improved considerably in recent decades, HRQOL has received increasing attention in pediatric oncology. Accordingly, general studies have been conducted relating factors of HRQOL to IQ and have found a significant relationship; however, few studies have investigated the relationship of specific intelligence functions with specific domains of HRQOL.

The present study has several limitations. Firstly, the participant number was small due to the low prevalence of childhood brain tumors. It will be necessary to confirm these results in an expanded patient group in a future study. Secondly, even though a majority of the patients completed their T1 assessment before radiotherapy, there was still conflict in the ordering of T1 assessment that may have influenced study findings. Thirdly, we did not conduct a long-term follow-up after treatment termination, and thus, could not evaluate later effects.

Despite these limitations, our results nevertheless show that intelligence significantly declined between on-treatment...
and off-treatment and that higher intelligence functioning in both periods was positively correlated with a higher HRQOL off treatment. In other words, higher intelligence was associated with a better quality of life in the long term. Further investigations that monitor intelligence functioning, HRQOL and parenting stress over a more sustained period are needed.

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