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Emotional and Behavioral Functioning After Conformal Radiation Therapy for Pediatric Ependymoma

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Abstract

Purpose/Objectives—The standard of care for pediatric patients with ependymoma involves post-operative radiation therapy. Prior research suggests that conformal radiation therapy (CRT) is associated with relative sparing of cognitive and academic functioning, but little is known about CRT's effect on emotional and behavioral functioning.

Methods and Materials—A total of 113 patients with pediatric ependymoma underwent CRT using photons as part of their enrollment on an institutional trial. Patients completed annual evaluations of neurocognitive functioning during the first five years after CRT. Emotional and behavioral functioning was assessed via the Child Behavior Checklist.

Results—Prior to CRT, emotional and behavioral functioning was commensurate with that of the normative population and within normal limits. After 5-years, means remained within normal limits but were significantly below the normative mean. Linear mixed models revealed a significant increase in attention problems over time. These problems were associated with age at diagnosis/CRT, tumor location, and extent of resection. A higher-than-expected incidence of school problems was present at all assessment points after baseline.

Conclusions—The use of photon CRT for ependymoma is associated with relatively stable emotional and behavioral functioning during the first five years after treatment. The exception is an increase in attention problems. Results suggest that intervening earlier in the survivorship period – during the first year post-treatment – may be beneficial.

Keywords

ependymoma; conformal radiation therapy; emotional and behavioral functioning; pediatric brain tumors

Ependymoma accounts for approximately 9% of pediatric brain tumors and is the third most common malignant tumor of childhood. This tumor typically arises in the posterior fossa

and is most often diagnosed in children younger than 4 years. Treatment usually involves surgical resection followed by post-operative radiation therapy, and survival rates are approximately 75% [1]. During the last decade, investigators have attempted to reduce the volume targeted for radiation therapy to reduce the functional effect of treatment while still maintaining high survival rates. The current standard of care involves the use of 3-dimensional methods of irradiation using photons or protons. The goal of using these methods is to spare healthy tissues while providing a therapeutic dose of radiation to the tumor bed [2].

Despite improvements in treatment protocols, the potential to affect function in patients with ependymoma, especially cognitive, emotional and behavioral function, remains high [3]. This is particularly true because of the young age at which most patients' tumors are diagnosed and treated. Results of prior studies suggest that using photon methods of conformal radiation therapy (CRT) is associated with relative sparing of many cognitive and academic skills [4,5] as well as adaptive functioning [6]; however, it is unknown whether this same protection is afforded to emotional and behavioral functioning.

Diagnosis and treatment of a brain tumor in childhood can be associated with declines in emotional and behavioral functioning. Specifically, prior research suggests that survivors are at risk for the development of attention problems [7,8], social problems [9,10], and emotional problems such as anxiety and depression [11]. Such difficulties coincide with declines in cognitive and academic functioning over time [12,13] and have been tied to changes in cerebral white matter that result from radiation therapy and chemotherapy [14,15]. Little is known about the longitudinal trajectory of emotional and behavioral functioning because prior studies have typically focused on assessment of long-term survivors. To understand the development of these deficits, it is important to examine the course of functioning over time.

Longitudinal studies of emotional and behavioral functioning in pediatric patients with brain tumors are rare. Completed studies have limitations reducing their results' generalizability, including small sample sizes [16,17], focusing only on a short time period [18], or having few observations [16,17]. Moreover, few researchers have completed serial assessments with patients from diagnosis into the off-treatment period, limiting our understanding of the trajectory of emotional and behavioral functioning over time. One recent study analyzed the longitudinal trajectory of social functioning in pediatric patients with medulloblastoma during the first five years after diagnosis [19]. This study's results demonstrated relatively stable functioning, though with higher proportions of patients experiencing clinically significant difficulties than would be expected, and declines associated with more intense central nervous system treatment [19]. Although this study was one of the first to examine the emotional and behavioral functioning of pediatric brain tumor patients over time, it was limited by its focus on social functioning, with little attention paid to other indices of emotional and behavioral functioning, including internalizing and externalizing behaviors.

Longitudinal studies provide rich data about the development of difficulties in survivors and will help determine opportune times to launch targeted interventions. The objective of the current study was to prospectively assess the emotional and behavioral functioning of

children with ependymoma during the first five years after photon-based CRT. Additionally, we aimed to determine whether certain demographic and clinical factors are associated with susceptibility to deficits in functioning. We hypothesized that patients would demonstrate a decline in emotional and behavioral functioning over time and that patients with greater neurological impact (e.g., shunted hydrocephalus, multiple surgeries), would experience greater declines in functioning.

Methods

Participants

The current study included 147 patients enrolled on an institutional phase II protocol of CRT for localized ependymoma. Patients were enrolled between July 1997 and January 2008. Inclusion criteria for the treatment protocol were as follows: aged 1 to 25 years at time of study entry, histologic confirmation of ependymoma, no evidence of metastatic disease, no ongoing chemotherapy, and no prior treatment with irradiation. Serial neurocognitive assessments were conducted at baseline (pre-CRT but post-surgery), 6 months post-CRT, and yearly thereafter for 5 years. The study was approved by the institution's IRB, and all patients or guardians provided informed consent.

For the current study, participants must have completed at least 2 neurocognitive assessments that included the Child Behavior Checklist (CBCL) [20], which is applicable for children between 4- and 18-years of age. Participation in assessments required that patients (and parents) spoke English as a primary language and had no sensory or motor impairment that would prohibit valid neurocognitive assessment. However, no patients were excluded for these reasons. The median number of completed CBCLs was 4 (range 2 – 7). Of note, 34 patients (23.1%) did not meet inclusion criteria for the current analysis, resulting in a final sample of 113 patients. Of those not included, 31 patients (91.2%) completed no assessments and 3 (8.8%) completed only one. Typical reasons for not completing assessments included age (too young or too old) or being taken off-study due to progressive disease. There were generally no significant differences between the demographic and treatment variables of those who were included in analyses and those who were not, except that patients not included were slightly more likely to have received chemotherapy prior to CRT ($p = .04$).

Radiation Therapy Parameters

All patients underwent surgical resection prior to CRT, with additional surgeries performed to maximize the extent of resection. Radiation treatment parameters have been previously described [21]. Briefly, all participants were treated by using conventional fractionation (1.8 Gy per day) with a prescribed dose of 59.4 Gy. Children younger than 18 months at treatment ($n = 16$, 14.2%) received a CRT dose attenuated to 54 Gy.

Serial Neurocognitive Assessments

Estimated intellectual function was assessed via the age-appropriate Wechsler scale: Preschool and Primary (ages 4–6; WPPSI-R, [22]), Child (ages 6–16; WISC-III, [23]) and Adult (age 16+; WAIS-III, [24]). The Block Design, Similarities, and Information subtests

were used to derive an estimate of IQ using a formula provided by Sattler [25] that yields an estimated IQ score that is highly correlated with the full-scale IQ scores ($r = .93$). All measures yield an age-normalized standard score with a mean of 100 and a standard deviation of 15.

Emotional and behavioral functioning was assessed by administering the CBCL [20]. The CBCL is a parent-report measure of emotional and behavioral functioning for children aged 4 to 18 years. Parents respond to several open-ended and forced-choice questions describing their child's social, academic, emotional, and behavioral functioning. A number of subscales are derived from these questions. Specifically, Competence Scores are computed to describe children's performance in school and social situations, and Clinical Scales are computed to describe several areas of emotional and behavioral functioning, including anxiety, depression, attention, etc. All scales yield age-normalized T-scores with a mean of 50 and standard deviation of 10. The following primary scales-of-interest were included: two summary Clinical Scales (Internalizing Problems and Externalizing Problems), three Competence Scales (Activities, Social Competence and School Competence), and two additional subscales of theoretical interest that are not included in the summary scores (Attention Problems and Social Problems). Notably, interpretation of T-scores varies by scale. Specifically, higher scores on the Clinical Scales (T-scores above 63) and the additional scales (Attention and Social Problems; T scores above 65) are indicative of greater problems and thus considered outside normal limits. In contrast, lower scores on the Competence Scales (T scores below 35) are indicative of greater concerns. The CBCL was the primary measure-of-interest for the current study. Additional measures administered during these evaluations, including assessment of academic achievement, attention problems, learning, and adaptive functioning, have been previously reported [4,6,26,27].

Analyses

Descriptive analyses were conducted to characterize the demographic, diagnostic, and treatment-related features of the patients at baseline. One-sample t-tests were used to compare the mean scores with normative means. Linear mixed models were used to investigate the change in CBCL indices-of-interest during the study. Subsequently, relevant demographic and clinical variables were added, one at a time, to investigate the effects of that variable on the longitudinal trajectory of the CBCL. Frequencies were calculated to determine proportions of the sample that exceeded expected clinical cut-offs on the CBCL.

Results

Patient Characteristics

Demographic and clinical characteristics of the 113 patients included in the current study are in Table I. The sample was relatively balanced with respect to clinical variables. At baseline, mean estimated IQ fell within normal limits but was significantly below the normative mean ($p = .0005$).

Emotional and Behavioral Functioning Over Time

Baseline and Year 5 scores on the CBCL for the scales-of-interest are presented in Table II. At baseline, all mean scores fell within normal limits and were not significantly different from the normative mean. In contrast, at Year 5, all scores were significantly different than the normative mean. Specifically, patients experienced fewer Internalizing Problems (e.g., anxiety, withdrawal) and fewer Externalizing Problems (e.g., aggressive or delinquent behavior) than the normative group. In contrast, patients exhibited decreased Activities, Social Competence, and School Competence, and greater Attention and Social Problems than did the normative group. Notably, mean scores remained within normal limits and were not considered to be elevated to either the Borderline or Clinical range.

Linear mixed models were used to determine the longitudinal trajectory of each CBCL scale over time. Results revealed that the observable change in scores during the 5-year period was not statistically significant for the majority of subscales (Table II; Figure 1). The exception was the Attention Problems subscale, which significantly increased over time, with an estimated slope of 0.779 points per year (intercept = 51.97, 95% CI = 0.1214 – 1.4365, $p = .021$; Figure 1a). Analyses were then conducted to determine the variability in the development of attention problems caused by key medical and demographic predictors. Results revealed that tumor location, extent of surgical resection, age at diagnosis, and age at CRT contributed significantly to the development of attention problems, with predictors affecting both baseline performance and the slope of incline or decline (Figure 2).

Specifically, the rate of increase of attention problems over time appeared to differ by tumor location: patients with tumors in the posterior fossa ($n = 87$) had increases of 0.844 ($p = .025$), tumors in the hemispheres ($n = 19$) demonstrated increases of 0.201 (NS) and those with centrally-located tumors ($n = 6$) increased approximately 3.292 points per year ($p = 0.019$). Patients who received a subtotal resection ($n = 10$) experienced minimal attention problems at baseline, but the rate of increase over time was significant, estimated at 3.22 points per year ($p = .003$). In contrast, patients who underwent gross-total resection ($n = 93$) had more attention problems at baseline, but their problems did not increase as much over time as did those who underwent other types of resections, with an estimated increase of 0.61 points per year. Additionally, patients who received a near-total resection ($n = 10$) had the most attention problems at baseline, but these issues declined subtly over time, estimated at a reduction in attention problems of 0.61 points per year. Furthermore, patients who were younger at diagnosis (intercept = 49.36, slope = -0.189 , $p = .032$) and at treatment (intercept = 49.24, slope = -0.186 , $p = .037$) experienced more attention problems over time than did older patients.

Age at diagnosis and age at irradiation were highly correlated ($r = 0.97$, $p < 0.0001$) because the majority of patients received radiation therapy shortly after diagnosis. Additionally, tumor location was associated with two other treatment-related variables: surgical extent ($p = .042$) and age at irradiation ($p = .026$).

Patients within the Clinical Range on Variables-of-Interest

Analyses were conducted to compare the percentage of patients at each time point that had clinically significant difficulties (e.g., outside normal limits) to the expected percentage for the normative sample. The percentages of patients having difficulties in the Clinical Range for Internalizing and Externalizing Problems or Social Problems were not significantly greater than the target percentage at any time point. However, more patients than expected were in the Clinical Range for Attention Problems at 12 and 60 months post-CRT.

As can be seen in Figure 3, a significantly greater proportion of patients was within the Clinical Range for many of the competence scales. Specifically, patients were engaged in fewer activities 5 years after treatment, had more difficulty with school at every assessment but baseline (at which point no patient was within the Clinical Range), and engaged in fewer social interactions than expected 1 year after CRT.

Discussion

Our objective was to examine the longitudinal trajectory of emotional and behavioral functioning in pediatric patients with ependymoma during the first five years after diagnosis. In contrast to expectations, patients demonstrated relative stability in emotional and behavioral functioning during these years. The exception, consistent with the extant literature, was attention problems, which increased significantly over time. These findings add to a growing body of literature suggesting that conformal and intensity-modulated radiation therapy lead to a relative sparing of cognitive, academic, and adaptive functioning in pediatric patients [4,6].

Despite the overall stability in emotional and behavioral functioning, patients with ependymoma are more likely to exhibit clinically significant levels of school problems than are a normative sample of their peers, and this difference persisted throughout the course of the study. The School Competence scale includes parent-reported information about the child's performance in academic subjects, participation in special education, and history of grade retention [20]. Therefore, our findings of school problems in this population might indicate that, despite previous research suggesting sparing of objective indicators of academic achievement [4], these survivors are exhibiting more school-related problems than would be expected, suggesting a need for earlier provision of special education services for survivors as well as a need to evaluate classroom functioning in conjunction with more objective measures of academic achievement. It may be that our traditional objective measures of academic functioning are not capturing the classroom behaviors and/or grade-based performances that were specified through this School Competence scale. Alternatively, these elevations may indicate that those patients who are in need of further accommodation and intervention in the classroom have not yet received these services. The School Competence scale from the CBCL may be able to serve as a screening tool to determine which patients need further objective assessment of cognitive and academic functioning. Further research would be needed to validate such usage of this tool.

Parent-reported attention problems increased significantly during the five-year study period, a finding that is commensurate with prior reports of declines in objective measures of

attention in this same population [26]. Several medical predictors were associated with development of attention problems, including tumor location, extent of surgical resection, and age at diagnosis/CRT. Attention problems are the most common cognitive late effect experienced by survivors of pediatric brain tumors. Moreover, these problems have been identified as a precursor to declines in cognitive and academic functioning and are associated with radiation therapy–caused white matter damage [28]. Given that many of the treatment-related predictors of attention problems were highly correlated, certain subsets of patients may be at increased risk for the development of attention problems, and closer monitoring may be warranted. These patients are potentially more neurologically compromised than are their peers and, thus, are at higher risk for the development of difficulties. Coupled with this, patients who are more neurologically-impaired may also be at greater risk for disfigurement and/or obesity [29], which may impact overall emotional and behavioral functioning, including the development of mood concerns or difficulties relating to peers. Notably, the risk factors identified in this study were also indicative of declines in adaptive functioning in this population [6].

Despite the significant increase in parent-rated attention problems, the overall mean remained solidly within normal limits at five years post-CRT. This may suggest that, although attention problems are increasing, they may not reach an impairing level at this time. Future studies of this cohort over a longer timeframe are needed to determine whether these early increases in attention problems predict later declines in cognitive or academic functioning. Moreover, because the mean age of these patients five years after CRT was still younger than 10 years, it remains to be seen what their functioning will be as they progress through the educational system.

This study has limitations. Specifically, the use of the CBCL with chronically ill populations has been cautioned against [30], as some evidence exists that there is limited variability within the normal range, which reduces the range of interpretable scores. This limitation may be one reason why mean Attention Problems scores remained within normal limits at five years post-CRT despite a significant increase over time. A second criticism of the CBCL is the inclusion of somatic concerns within the Internalizing Problems composite [30]. Indeed, chronically ill patients are more likely to have physical symptoms, most of which may not be related to their mood state but may artificially inflate their Internalizing Problems score. In this sample, no elevations in Internalizing Problems were noted at baseline or 5-years post-CRT, and no change was observed over time, suggesting that this criticism may not apply for this group of patients. Despite these concerns, the CBCL remains a frequently used tool for the broad assessment of emotional and behavioral functioning in chronically ill populations [31]. The study could have been strengthened if additional domain-specific measures of constructs-of-interest, such as the Conners Rating Scales [32] for attention problems, were used in conjunction. Finally, longitudinal research is often limited by drop-out and missing data; a limitation that was also applicable in this study. Our inclusion criteria only required two of a possible seven observations; the mean number of CBCLs completed per patient was approximately four.

This study supports prior research findings identifying attention problems as a major focus of intervention for pediatric patients with brain tumors. Indeed, several types of

interventions have focused on inattention, including stimulant medication [33], cognitive remediation [34], and computerized cognitive training [35]. Notably, these interventions are typically limited by their concentration on the survivorship period (e.g., patients who have been off-treatment and medically stable for at least one year). However, our results suggest that intervening during the first year off-treatment may be indicated. Indeed, examination of our clinical cut-off values suggests that a higher-than-expected proportion of patients are experiencing clinically significant attention problems at the 12-months post-CRT assessment. If we were to intervene earlier with these patients, we may be able to further minimize the development of attention problems and other late effects of CRT.

The results of this study support the use of photon-based CRT for patients with ependymoma to maximize survival and associated quality of life by showing that advanced methods of irradiation spare neurocognitive and emotional and behavioral functioning. These findings are particularly important because of the young age at which patients with ependymoma are treated. Future studies may consider more extended observations of these patients to confirm these early findings or to compare these results with those obtained by using even newer methods. Efforts at intervention, if not prevention, might be aimed at further reducing attention and school problems.

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References

1. Wright KD, Gajjar A. Current treatment options for pediatric and adult patients with ependymoma. *Curr Treat Options Oncol*. 2012; 13:465–477. [PubMed: 22798016]
2. Merchant TE. Three-dimensional conformal radiation therapy for ependymoma. *Childs Nerv Syst*. 2009; 25:1261–1268. [PubMed: 19373477]
3. Charalambides C, Dinopoulos A, Sgouros S. Neuropsychological sequelae and quality of life following treatment of posterior fossa ependymomas in children. *Childs Nerv Syst*. 2009; 25:1313–1320. [PubMed: 19554333]
4. Conklin HM, Li C, Xiong X, et al. Predicting change in academic abilities after conformal radiation therapy for localized ependymoma. *J Clin Oncol*. 2008; 26:3695–3970. [PubMed: 18669454]
5. Landau E, Boop FA, Conklin HM, et al. Supratentorial ependymoma: Disease control, complications, and functional outcomes after irradiation. *Int J Radiat Oncol Biol Phys*. 2013; 85:e193–199. [PubMed: 23245280]
6. Netson KL, Conklin HM, Wu S, et al. A 5-year investigation of children's adaptive functioning following conformal radiation therapy for localized ependymoma. *Int J Radiat Oncol Biol Phys*. 2012; 84:217–223. [PubMed: 22541967]
7. Brière M, Scott JG, McNall-Knapp RY, et al. Cognitive outcome in pediatric brain tumor survivors: Delayed attention deficit at long-term follow-up. *Pediatr Blood Cancer*. 2008; 50:337–340. [PubMed: 17458873]
8. Patel SK, Lai-Yates JJ, Anderson JW, et al. Attention dysfunction and parent reporting in children with brain tumors. *Pediatr Blood Cancer*. 2007; 49:970–974. [PubMed: 17243136]
9. Bonner MJ, Hardy KK, Willard VW, et al. Social functioning and facial expression recognition in survivors of pediatric brain tumors. *J Pediatr Psychol*. 2008; 33:1153–1162. [PubMed: 18400838]
10. Vannatta K, Gartstein MA, Short A, et al. A controlled study of peer relationships of children surviving brain tumors: Teacher, peer, and self ratings. *J Pediatr Psychol*. 1998; 23:279–287. [PubMed: 9782676]

11. Zeltzer LK, Recklitis C, Buchbinder D, et al. Psychological status in childhood cancer survivors: A report from the childhood cancer survivor study. *J Clin Oncol*. 2009; 27:2396–2404. [PubMed: 19255309]
12. Mulhern RK, Merchant TE, Gajjar A, et al. Late neurocognitive sequelae in survivors of brain tumors in childhood. *Lancet Oncol*. 2004; 5:399–408. [PubMed: 15231246]
13. Spiegler BJ, Bouffet E, Greenberg ML, et al. Change in neurocognitive functioning after treatment with cranial radiation in childhood. *J Clin Oncol*. 2004; 22:706–713. [PubMed: 14966095]
14. Khong P, Leung LHT, Fung ASM, et al. White matter anisotropy in post-treatment childhood cancer survivors: Preliminary evidence of association with neurocognitive functioning. *J Clin Oncol*. 2006; 24:884–890. [PubMed: 16484697]
15. Mabbott DJ, Noseworthy MD, Bouffet E, et al. Diffusion tensor imaging of white matter after cranial radiation in children with medulloblastoma: Correlation with iq. *Neuro Oncol*. 2006; 8:244–252. [PubMed: 16723629]
16. Sands SA, Pasichow KP, Weiss R, et al. Quality of life and behavioral follow-up study of head start i pediatric brain tumor survivors. *J Neurooncol*. 2011; 101:287–295. [PubMed: 20526792]
17. An KJ, Joung YS, Sung KW, et al. 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. *Yonsei Med J*. 2013; 54:306–314. [PubMed: 23364961]
18. Penn A, Lowis SP, Stevens MC, et al. A detailed prospective longitudinal assessment of health status in children with brain tumors in the first year after diagnosis. *J Pediatr Hematol Oncol*. 2011; 33:592–599. [PubMed: 21768887]
19. Brinkman TM, Palmer SL, Chen S, et al. Parent-reported social outcomes after treatment for pediatric embryonal tumors: A prospective longitudinal study. *J Clin Oncol*. 2012; 30:4134–4140. [PubMed: 23071220]
20. Achenbach, TM. Manual for the cbcl. Burlington, VT: University of Vermont; 1991.
21. Merchant TE, Xiong X, Kun LE, et al. Conformal radiotherapy after surgery for paediatric ependymoma: A prospective study. *Lancet Oncol*. 2009; 10:258–266. [PubMed: 19274783]
22. Wechsler, D. Wechsler preschool and primary scale of intelligence, revised. San Antonio, TX: The Psychological Corporation; 1989.
23. Wechsler, D. Wechsler intelligence scale for children. 3. San Antonio, TX: The Psychological Corporation; 1991.
24. Wechsler, D. Wechsler adult intelligence scale. 3. San Antonio, TX: The Psychological Corporation; 1997.
25. Sattler, JM. Assessment of children. San Diego: Jerome M. Sattler, Publisher Inc; 1992.
26. Kiehna EN, Mulhern RK, Li C, et al. Changes in attentional performance of children and young adults with localized primary brain tumors after conformal radiation therapy. *J Clin Oncol*. 2006; 24:5283–5290. [PubMed: 17114662]
27. Di Pinto M, Conklin HM, Li C, et al. Investigating verbal and visual auditory learning after conformal radiation therapy for childhood ependymoma. *Int J Radiat Oncol Biol Phys*. 2010; 77:1002–1008. [PubMed: 19783376]
28. Reddick WE, White HA, Glass JO, et al. Developmental model relating white matter volume to neurocognitive deficits in pediatric brain tumor survivors. *Cancer*. 2003; 97:2512–2519. [PubMed: 12733151]
29. Morris EB, Li C, Khan RB, et al. Evolution of neurological impairment in paediatric intracranial ependymoma patients. *J Neurooncol*. 2009; 94:391–398. [PubMed: 19330288]
30. Perrin EC, Stein REK, Drotar D. Cautions using the child behavior checklist: Observations based on research about children with a chronic illness. *J Pediatr Psychol*. 1991; 16:411–421. [PubMed: 1941423]
31. Pinquart M, Shen Y. Behavior problems in children and adolescents with chronic physical illness: A meta-analysis. *J Pediatr Psychol*. 2011; 36:1003–1016. [PubMed: 21810623]
32. Conners, CK. Conners rating scales. 3. Toronto, ON: Multi-Health Systems Inc; 2008.

33. Conklin HM, Reddick WE, Ashford J, et al. Long-term efficacy of methylphenidate in enhancing attention regulation, social skills, and academic abilities of childhood cancer survivors. *J Clin Oncol*. 2010; 28:4465–4472. [PubMed: 20837955]
34. Butler RW, Copeland DR, Fairclough DL, et al. A multicenter, randomized clinical trial of a cognitive remediation program for childhood survivors of a pediatric malignancy. *J Consult Clin Psychol*. 2008; 76:367–378. [PubMed: 18540731]
35. Hardy KK, Willard VW, Bonner MJ. Computerized cognitive training in survivors of childhood cancer: A pilot study. *J Pediatr Oncol Nurs*. 2011; 28:27–33. [PubMed: 20966158]

a) Emotional and Behavioral Functioning

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b) Competence Scales

Figure 1.

Longitudinal trajectory of emotional and behavioral functioning over time. *Note.* Figure 1a: For Internalizing and Externalizing Problems, higher scores are indicative of more problems. T-scores between 60 and 63 are in the Borderline Range, and above 63 are in the Clinic Range. For Attention and Social Problems, T-scores between 65 and 69 are in the Borderline range and 70 and above are in the Clinical range. Figure 1b: For Competence Scales, Lower scores are indicative of more problems. T-scores between 30 and 35 are in the Borderline range and scores below 30 are in the Clinical range.

Figure 2.

Effect of tumor location and extent of surgical resection on the development of attention problems over time. *Note.* Higher scores are indicative of more problems. T-scores between 65 and 69 are in the Borderline range and 70 and above are in the Clinical range.

Figure 3.

Percentage of scores within the Clinical Range (T -score < 30) on the Competence Scales at each time point. The solid line at 2.3% denotes expected proportion of scores in the normative sample that are within the Clinic Range.

Table I

Demographic and treatment characteristics

	N (%)	Mean (SD)	Range
Sex			
Male	60 (53.1)		
Female	53 (46.9)		
Race			
White	96 (85.0)		
Black	10 (8.9)		
Other	7 (6.1)		
Age at diagnosis (years)		4.49 (3.86)	0.20 – 16.81
Age at CRT (years)		4.95 (3.88)	1.02 – 16.89
Tumor Location			
Infratentorial	87 (77.0)		
Supratentorial	26 (23.0)		
Tumor Location*			
Central	6 (5.3)		
Hemispheric	19 (16.8)		
Posterior Fossa	87 (77.0)		
Pre-CRT Extent of Resection			
Gross-Total	93 (82.3)		
Near-Total	10 (8.8)		
Sub-Total	10 (8.8)		
Pre-CRT Number of Surgeries		1.46 (0.72)	1 – 5
1	72 (63.7)		
2	33 (29.2)		
3+	8 (7.1)		
Pre-CRT Chemotherapy	21 (18.6)		
VP-Shunt	39 (34.5)		
History of Seizures	20 (17.7)		
Baseline Estimated IQ [#]		93.40 (18.31)	50 – 148

Abbreviations: SD = standard deviation; CRT = conformal radiation therapy; VP = ventriculoperitoneal

* One of the supratentorial tumors could not be further categorized in this manner.

[#] Estimated IQ of the sample is significantly below the normative mean of 100, SD = 15; $p = .0005$

Table II

Emotional and behavioral functioning of children after conformal radiation therapy

Child Behavior Checklist Scales-of-Interest	Baseline		Year 5		Longitudinal Statistics	
	Mean (SD)	p-value*	Mean (SD)	p-value*	Annual Change	p-value ⁺
Summary Scales ^a						
Internalizing Problems	50.19 (11.66)	--	47.38 (10.48)	.029	-0.301	--
Externalizing Problems	47.03 (9.61)	--	44.18 (9.80)	<.001	-0.264	--
Competence Scales ^b						
Activities	48.52 (6.90)	--	46.69 (8.18)	.002	-0.031	--
School Competence	46.25 (8.28)	--	41.16 (9.25)	<.001	-0.401	--
Social Competence	48.73 (7.46)	--	45.18 (8.29)	<.001	-0.422	--
Individual Scales ^c						
Attention Problems	50.81 (15.72)	--	55.05 (6.95)	<.001	0.779	.021
Social Problems	50.73 (15.68)	--	53.44 (5.67)	<.001	0.117	--

* p-value indicates univariate analysis against normative mean of 50 (SD = 10)

⁺ p-value indicates significance of decline over time

-- non-significant

^a Borderline Range: 60–63; Clinical Range: >63; higher scores indicative of more problems^b Borderline Range: 30–35; Clinical Range: <30; lower scores indicative of more problems^c Borderline Range: 65–69; Clinical Range: >70; higher scores indicative of more problems