Cognitive Predictors of Social Adjustment in Pediatric Brain Tumor Survivors Treated with Photon versus Proton Radiation Therapy

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Abstract

Background: Pediatric brain tumor survivors are at risk for poor social outcomes. It remains unknown whether cognitive sparing with proton radiotherapy (PRT) supports better social outcomes relative to photon radiotherapy (XRT). We hypothesized that survivors treated with PRT would outperform those treated with XRT on measures of cognitive and social outcomes. Further, we hypothesized that cognitive performance would predict survivor social outcomes. Procedure: Survivors who underwent PRT (n=38) or XRT (n=20) participated in a neurocognitive evaluation >1 year post-radiotherapy. Group differences in cognitive and social functioning were assessed using ANCOVA. Regression analyses examined predictors of peer relations and social skills. Results: Age at evaluation, radiation dose, tumor diameter, and sex did not differ between groups (all $p>0.05$). However, XRT participants were younger at diagnosis (XRT M=5.0 years, PRT M=7.6 years) and further out from radiotherapy (XRT M=8.7 years, PRT M=4.6 years). The XRT group performed worse than the PRT group on measures of processing speed ($p=0.01$) and verbal memory ($p<0.01$); however, social outcomes did not differ by radiation type. The proportion of survivors with impairment in peer relations and social skills exceeded expectation (?2(1)=38.67, $p<0.001$; ?2(1)=5.63, $p<0.05$), and verbal memory approached significance as a unique predictor of peer relations (t=-2.01, $p=0.05$). Total tumor RT dose significantly predicted social skills (t=-2.23, $p<0.05$). Conclusions: Regardless of radiation modality, survivors are at risk for social challenges, with one-quarter being socially excluded or undervalued. Deficits in verbal memory may place survivors at particular risk. Results support monitoring of cognitive and social functioning throughout survivorship.

Introduction

It is well documented that pediatric brain tumor survivors are at risk for poor long-term social outcomes relative to same-age peers. Reviews of social outcomes in survivors have highlighted an increased risk for social skill deficits and poor long-term social adjustment, including social isolation and victimization.[1,2] Recent studies examining specific components of social adjustment, such as peer relationships, have found that survivors are less likely to be able to name a friend than children with non-central nervous system tumors[3] and are at high risk of having no reciprocated best friendship nominations in sociometric analyses.[4]Caregiver

ratings also highlight social concerns among survivors, with poor social outcomes rated as among the most impactful late effects in survivorship.[5] This has prompted recent intervention efforts to support survivor social skills and overall social functioning.[6,7] However, much remains unknown with respect to predictors of social adjustment among survivors.

Given known cognitive deficits following cancer and cancer-related treatments,[8] as well as the known interrelationship of cognitive and social functioning, [9,10] it is likely that cognitive skills are drivers of survivor social outcomes. In fact, a recent review highlighted the identification of determinants of social impairment as one of the most important emerging areas in survivorship research in this population.[11] Schulte and colleagues[12] found that cognitive impairment mediated the association between cranial radiation therapy and survivor social outcomes, including quality of social interactions and social withdrawal. Other researchers have examined more specific cognitive outcomes. For example, Dejardins and colleagues[13]found an association between metacognitive skills and parent ratings of survivor social skills (e.g., cooperation, assertiveness, and self-control). Studies have also examined attention skills as important predictors of social outcomes, highlighting inattention and parent-reported attention problems as significant predictors of survivor social problems.[14,15] Continued investigation into known cognitive skill deficits among survivors (e.g., processing speed, executive functioning) and the impact of these deficits on specific aspects of social functioning is warranted, particularly given known associations between cognitive predictors and social outcomes in other pediatric traumatic and acquired brain injury populations[16-18] as well as autism spectrum disorder.[19, 20]

In addition to examining specific cognitive predictors, an investigation of survivor social outcomes should consider different radiation treatment modalities and the neurocognitive sparing potential of proton radiation therapy (PRT). Given the unique physical properties of PRT, maximum radiation dose is delivered to the tumor, with less entrance dose and no exit dose compared to photon radiation (XRT).[21-23] Thus, with the sparing of more healthy brain tissue, it is suggested that PRT may yield better neurocognitive outcomes compared to XRT. The few comparison studies published to date are suggestive of neurocognitive sparing with PRT, with evidence for higher IQ, processing speed, perceptual reasoning, executive functioning, and fine motor coordination among survivors treated with PRT versus XRT.[24-27] However, continued comparison of clinically meaningful outcomes across radiation groups is warranted.

Of these clinically meaningful outcomes, social functioning remains particularly understudied. If indeed PRT offers a neuroprotective benefit over XRT, it is plausible that better neurocognitive outcomes among survivors treated with PRT would support better social outcomes compared to those treated with XRT. However, this relationship between therapy modality, neurocognitive outcomes, and social functioning has not been directly examined. In their recent study comparing PRT and XRT treatment groups, Gross and colleagues[26] found better parent-rated social functioning for patients treated with PRT relative to XRT on a broadband adaptive skills rating measure. In another study examining quality of life more broadly, PRT patients were found to have higher quality of life ratings in the psychosocial domain relative to XRT patients.[28] While these findings are promising, cognitive predictors were not examined.

The present study offers the first known examination of a wide range of neurocognitive skills as predictors of peer relationships and social skills between pediatric brain tumor survivors treated with PRT versus XRT in late survivorship. We hypothesized that survivors treated with PRT would outperform those treated with XRT on cognitive measures and would be rated by caregivers as having better social outcomes. We also hypothesized that cognitive outcomes would predict survivor peer relations and social skills.

Methods

Participants

Participants were part of a larger study examining long-term neurocognitive, social-emotional, and functional outcomes in pediatric brain tumor survivors. Participants were enrolled according to the following eligibility criteria: (1) treated with a single course of PRT or XRT for a primary brain tumor, (2) no evidence of active disease at enrollment, (3) age [?] 6 years at evaluation, and (4) fluent in English. All participants treated with XRT were treated between 2001 and 2006, while those treated with PRT were treated between

2007 and 2013. The timing defined for the two RT groups differed due to a shift from XRT to PRT as standard of care in 2007 at our institution. Eligible participants for the parent study were identified via medical record review and were approached for enrollment between 2011 and 2018. An 87.3% participation rate was achieved for the study. Patients who declined participation did not significantly differ from enrolled participants based on RT type, sex, race, or histology (data not shown, all $p > 0.05$). Of note, given our interest in long-term neurocognitive and social outcomes, patients diagnosed with brain stem glioma, high-grade glioma, or atypical teratoid/rhabdoid tumors were excluded from participation. Data were also excluded for participants who could not complete testing due to profound cognitive or visual impairment (n=5). The present study reports on the outcomes of 58 patients. Medical and demographic characteristics for participants are reported in Table 1.

Measures

At the time of evaluation, all participants completed a neurocognitive battery with age-appropriate standardized measures. Parent-, teacher-, and self-report norm-referenced rating measures were also provided, as appropriate. Relevant variables for the present study are delineated in Table 2. Participant peer relations and social skills were assessed using the Conners 3 and BASC-3 rating forms, respectively. The Peer Relations scale provides an estimate of the quality of friendships maintained by the child and the extent to which the child appears to be accepted by his or her peer group.[29] As a separate measure of social functioning, the BASC-3 Social Skills scale provides an estimate of a child's ability to interact successfully with peers and adults in the home, school, and community settings.[30]Additionally, the following cognitive variables were assessed: processing speed, executive functioning, verbal learning, verbal memory, sustained attention, and overall intellectual functioning. Several standardized measures were administered to assess different aspects of executive functioning, including cognitive flexibility and inhibition. These measures were combined into an executive function composite (see Table 2). Standardized scores (standard score, T-scores, scaled scores, z-scores) were computed using age norms for all measures. Of note, all evaluations were conducted prior to the onset of the COVID-19 pandemic; therefore, standardized administration procedures and childhood social opportunities were not impacted by changes in procedures and enhanced safety precautions resulting from the pandemic.

Statistical Analyses

Demographic and clinical factors were compared by radiation type (XRT vs PRT) using Chi Square, Fisher exact test, or independent t -tests, as appropriate. Group differences in social functioning and cognitive functioning were assessed using analysis of covariance (ANCOVA), covarying for the effects of time since radiation. Because peer relations and social skills did not differ by radiation type, remaining analyses examined the sample as a whole. To evaluate social outcomes among pediatric brain tumor survivors, one-sample t-tests compared peer relations and social skills with the normative mean of 50. Frequency data on the number of participants rated as having impaired social outcomes were examined, with impairment defined as scores falling 1.5 SD above the mean for peer relations (i.e. $<$ standard score of 65) and 1.5 SD below the mean for social skills (i.e.$>$ standard score of 35). Further, χ^2 analyses determined whether the percentage of participants with impairment exceeded expectation assuming normal distribution of scores (6.68%). Bivariate correlations were run to examine relationships between social outcomes and demographic, clinical, and cognitive variables. Predictors were included in multiple linear regression analyses based on significant correlations with peer relations and social skills. Demographic and clinical variables that were significantly correlated ($p < 0.05$) with the specific outcome were included in the models. Cognitive skills that significantly correlated with either peer relations or social skills were also included (processing speed, executive functioning, verbal memory, and sustained attention).

Results

Demographic and Clinical Characteristics

Comparisons of demographic and clinical characteristics between survivors treated with XRT and PRT are displayed in Table 1. The XRT group was younger on average at diagnosis than the PRT group ($p< 0.01$).

Reflecting the study design, the XRT group was further out from RT completion at the time of neurocognitive evaluation relative to the PRT group ($p < 0.001$). Both groups were made up of predominantly male survivors, and the majority of primary caregivers completed high school at a minimum. The majority of survivors in both groups underwent craniotomy and similar rates were treated with craniospinal radiation (60% of the XRT group and 55% of the PRT group).

Cognitive and Social Outcomes in Survivors Treated with XRT versus PRT

Comparisons of social and cognitive outcomes between survivors treated with XRT and PRT accounting for time since radiation are presented in Table 3. Peer relations and social skills were similar across RT groups (all F s < 1, p s $> .8$). The average IQ score of the XRT group fell in the Below Average range of ability and was significantly lower than that of the PRT group, which was Average (p <0 .01). Cognitively, the XRT group performed significantly worse than the PRT group on measures of processing speed ($p = 0.01$) and verbal memory ($p < 0.01$). Effects for executive functioning ($p = 0.06$) and verbal learning ($p = 0.07$) approached significance. Survivors treated with XRT and PRT performed similarly on a measure of sustained attention.

Social Skills and Peer Relations among Survivors of Pediatric Brain Tumor

Because peer relations and social skills did not differ by radiation type, remaining analyses examined the sample as a whole. As a group, survivors of pediatric brain tumor were rated as having more difficulties with peer relations (M = 57.52, SD = 18.89) relative to the normative mean of 50, t (57) = 3.03, $p < 0.01$, though increased difficulties were not observed for social skills (M = 50.93, SD = 10.59), t (56) = 0.66, $p = 0.51$. However, the percentage of participants meeting criteria for impairment in peer relations (27.6%) and social skills (12.1%) exceeded expectation (i.e., 6.68%), ($\chi^2(1) = 38.67$, $p < 0.001$; $\chi^2(1) = 5.63$, $p < 0.05$).

Item level analysis of all six items from the parent-report version of the Conners 3 Peer Relations scale indicated that 22% of pediatric brain tumor survivors are “often” or “very often” not invited to play or go out with others, and 27% are among the last to be selected for team games. Further, parent ratings indicated that 9% of survivors have no friends and do not know how to make friends. On the BASC-3 Social Skills scale, approximately half of survivors (45-51%) were rated as “never” or only “sometimes” demonstrating prosocial social skills such as complimenting others, showing interest in the ideas of others, and volunteering to help others (see Table 4).

Correlates of Social Functioning among Survivors of Pediatric Brain Tumor

Correlations among predictors (demographic/clinical and cognitive) and social outcomes yielded a number of significant relationships (see Table 5). Increased difficulties on the Peer Relations subscale was significantly correlated with longer time since radiation ($p< 0.05$) and shunt placement ($p < 0.01$). Increased social skill problems were significantly correlated with larger tumor diameter ($p < 0.05$). Slower processing speed, reduced executive functioning, and poorer verbal memory were all significantly correlated with increased difficulties with peer relations. Reduced social skills was significantly correlated with slower processing speed alone.

Multiple linear regression models examined the independent and shared contributions of predictors that were significant in univariate correlations with outcomes (see Table 6). For peer relations, the overall model was significant, F (6, 51) = 3.94, $p< 0.01$, with verbal memory approaching significance as a unique predictor, t = -2.01, $p = 0.05$. For social skills, the overall model was significant F (5, 51) = 2.40, $p = 0.05$, and maximum tumor diameter emerged as the only significant unique predictor, t = -2.23, $p < 0.05$.

Discussion

Consistent with previous studies, the present findings highlight social difficulties among pediatric brain tumor survivors. Peer relationships (i.e., friendship quality, acceptance by peers) emerged as an area of particular concern. Significantly more survivors were rated as having difficulties with peer relations relative to normative expectation, with a sizable portion of pediatric brain tumor survivors (˜25%) experiencing

social exclusion (e.g., not being invited to play, selected last for team games). These findings broadly correspond with previous research highlighting survivor vulnerability to peer exclusion and isolation. [31,32] Further, a relatively small but remarkable number of survivors (˜10%) were rated by caregivers as having no friendships. These results are similar to previous findings,[3,33] although Hocking and colleagues reported a greater proportion of survivors (38%) who were unable to name a friend.

The proportion of survivors experiencing problems with social skills also significantly differed between survivors and normative expectations, which is consistent with previous findings documenting social skill deficits among pediatric brain tumor survivors[2,32]. Specific prosocial skills, such as complimenting others and offering to help, emerged as areas of difficulty on individual item review in the present study. Ultimately, the results encourage continued efforts to better understand and support survivor social functioning.

In examining associations between social and cognitive outcomes, the current findings identify several cognitive variables as potentially influential for peer relations and social skills among pediatric brain tumor survivors. Processing speed, an area in which survivors consistently demonstrate impairment, [34-36]significantly correlated with both peer relationships and social skills. Executive functioning and verbal memory also correlated significantly with peer relations. However, no cognitive variables significantly predicted social skills, and only verbal memory approached significance as a unique predictor of peer relations in the context of other cognitive and treatment variables in the regression model. The fact that verbal memory approached significance as a unique predictor of peer relations is not surprising given the role of verbal memory in language processing and social communication, facilitating the retrieval of previously learned verbal information and incorporation of such information with conversational demands. [37] However, while verbal memory correlates with social problem solving and caregiver-reported social skills in other medical populations (e.g., traumatic brain injury[38]), the relationship between verbal memory and social outcomes has not been closely examined in the pediatric brain tumor population. As verbal memory is known to be at risk in brain tumor survivors, likely as a result of disease and treatment-related damage to temporal structures and cortical connectivity underlying memory function,[39] this relationship warrants further investigation.

It is notable that survivor social outcomes did not differ based on RT modality, although significant differences in cognitive outcomes between survivors treated with XRT versus PRT extend previous studies suggesting a potential neuroprotective benefit of PRT for cognitive skills.[24-27] Given previous associations of cognitive impairment with poor social outcomes,[12] it was expected that the XRT group would have significantly lower social outcomes than the PRT group as a function of lower cognitive performance. Indeed, Gross and colleagues[26] identified significant differences between radiation groups on a measure of adaptive social functioning, suggesting that survivors treated with PRT have more favorable social outcomes relatives to those treated with XRT. However, the present findings suggest that RT modality may be a less important driver of long-term social outcomes than other treatment variables. Longer time since RT and shunt placement were significant correlates of survivor peer relation difficulties, and tumor diameter emerged as a significant predictor of social skills in the multiple linear regression model. These results echo early findings of worse parent-rated social skills for survivors with greater time since diagnosis[40] and suggest that disease factors and illness complications (e.g., tumor size, hydrocephalus) are impactful for long-term social outcomes, potentially more so than RT modality. Further investigations will benefit from consideration of specific treatment factors as well as broader aspects of brain tumor diagnosis and treatment (e.g., school absences, internalizing and externalizing symptoms associated with medical trauma, changes in family dynamics) as potentially meaningful influencers of survivor social outcomes.

The present study has several clinical implications. First, the social challenges observed in the present sample were documented at long-term follow-up, indicating that late effects of brain tumor diagnosis and treatment likely include social deficits that occur well into survivorship. Further, the finding of social difficulties among survivors in both RT groups supports the need for careful monitoring of social adjustment regardless of radiation modality. Models and guidelines for the neuropsychological care of survivors[41] should therefore emphasize continued surveillance and monitoring of social functioning, even in light of potential neurocognitive sparing associated with PRT. The recent social limitations and isolation resulting from COVID-19

precautions likely place survivors at even greater risk for social adjustment challenges. Additionally, results suggest that survivors with cognitive impairments at follow-up, particularly in verbal memory, may be at heightened risk for social difficulties. It is also notable that peer relations, not social skills, emerged as the greater area of concern for survivors. This encourages careful consideration of assessment methods, with measures that directly inquire about friendships and social acceptance potentially capturing a broader picture of survivor social functioning than those evaluating social skills. Direct questions regarding survivor friendships in an interview format, such as the approach utilized by Hocking and colleagues, [3] may also provide opportunities to offer clarification and thereby identify a greater number of survivors with social difficulties compared to parent rating measures alone.

Limitations

Readers should note several study limitations. Given the practical and ethical barriers preventing a randomized controlled trial in this sample, patients were not randomized to RT groups. It should also be noted that RT groups differed with respect to the follow-up interval, as PRT patients were treated more recently than XRT patients. We attempted to minimize this difference by examining the last available cohort of XRT patients and the first available cohort of PRT patients. Further, the cross-sectional study design precludes direct analysis of changes in cognitive and social functioning over time. It should also be noted that families with greater concerns regarding their child's outcomes may be more likely to remain engaged in follow-up through pediatric oncology centers, which may result in a sample with more cognitive or functional difficulties. The small sample size is another limitation for the present study, potentially affecting our ability to detect significant differences and significant predictors in some instances. Regarding measurement, it is notable that the present study incorporated only parent report measures for the assessment of social outcomes. Although parent report measures provide meaningful information and are commonly used as screening measures in clinical settings, other studies have noted the benefits of sociometric approaches (e.g., peer nominations), computer-based measures of social information processing, and interviews for the evaluation of survivor social outcomes.[3,4,42,43]

Conclusions

Regardless of radiation modality, pediatric brain tumor survivors are at risk for long-term social difficulties, with perceived friendship quality and peer acceptance being areas of particular vulnerability. Survivors are also at risk for cognitive late effects, and those with weaknesses in verbal memory may be at higher risk for peer relationship challenges. Treatment variables such as time since radiation, hydrocephalus/shunt placement, and tumor diameter may prove more influential for long-term social functioning than radiation modality, although further investigation is needed. Overall, survivors will benefit from continued monitoring of cognitive and social functioning over the course of survivorship. It is hoped that further inquiry into cognitive and clinical predictors of social outcomes will inform interventions to support survivor social adjustment and overall quality of life.

Conflict of Interest

The authors declare that there is no conflict of interest.

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Data Availability Statement

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

References

1. Schulte F. Social competence in pediatric brain tumor survivors: breadth versus depth. *Current Opinion in Oncology.*2015;27(4):306-310.

2. Hocking MC, McCurdy M, Turner E, et al. Social competence in pediatric brain tumor survivors: Application of a model from social neuroscience and developmental psychology. *Pediatric Blood & Cancer.* 2015;62(3):375-384.

3. Hocking MC, Noll RB, Kazak AE, Brodsky C, Phillips P, Barakat LP. Friendships in Pediatric Brain Tumor Survivors and Non-Central Nervous System Tumor Survivors. *Journal of Pediatric Psychology.*2020;45(2):194-202.

4. Desjardins L, Barrera M, Chung J, et al. Are we friends? Best friend nominations in pediatric brain tumor survivors and associated factors.*Supportive Care in Cancer.* 2019;27(11):4237-4244.

5. Henrich N, Marra CA, Gastonguay L, et al. De-escalation of therapy for pediatric medulloblastoma: trade-offs between quality of life and survival. *Pediatric blood & cancer.* 2014;61(7):1300-1304.

6. Willard VW. Social skills interventions for survivors of pediatric brain tumors: A review and reformulation. *Pediatric blood & cancer.* 2018;65(12):e27434.

7. Schulte F, Vannatta K, Barrera M. Social problem solving and social performance after a group social skills intervention for childhood brain tumor survivors. *Psycho-Oncology.* 2014;23(2):183-189.

8. Ullrich NJ, Embry L. Neurocognitive dysfunction in survivors of childhood brain tumors. Paper presented at: Seminars in pediatric neurology2012.

9. Moyer KH, Willard VW, Gross AM, et al. The impact of attention on social functioning in survivors of pediatric acute lymphoblastic leukemia and brain tumors. *Pediatric blood & cancer.*2012;59(7):1290-1295.

10. McQuade JD, Murray-Close D, Shoulberg EK, Hoza B. Working memory and social functioning in children. *Journal of experimental child psychology.* 2013;115(3):422-435.

11. Oyefiade A, Paltin I, De Luca CR, et al. Cognitive risk in survivors of pediatric brain tumors. *Journal of clinical oncology: official journal of the American Society of Clinical Oncology.*2021;39(16):1718-1726.

12. Schulte F, Brinkman TM, Li C, et al. Social adjustment in adolescent survivors of pediatric central nervous system tumors: A report from the C hildhood C ancer S urvivor S tudy. *Cancer.*2018;124(17):3596-3608.

13. Desjardins L, Solomon A, Janzen L, et al. Executive functions and social skills in pediatric brain tumor survivors. *Applied Neuropsychology: Child.* 2020;9(1):83-91.

14. Willard VW, Allen TM, Hardy KK, Bonner MJ. Social functioning in survivors of pediatric brain tumors: Contribution of neurocognitive and social-cognitive skills. *Children's Health Care.*2017;46(2):181-195.

15. Holland AA, Colaluca B, Bailey L, Stavinoha PL. Impact of attention on social functioning in pediatric medulloblastoma survivors.*Pediatric hematology and oncology.* 2018;35(1):76-89.

16. Anderson V, Beauchamp MH, Yeates KO, et al. Social competence at two years after childhood traumatic brain injury. *Journal of neurotrauma.* 2017;34(14):2261-2271.

17. Robinson KE, Fountain-Zaragoza S, Dennis M, et al. Executive functions and theory of mind as predictors of social adjustment in childhood traumatic brain injury. *Journal of Neurotrauma.*2014;31(22):1835-1842.

18. Greenham M, Gordon AL, Cooper A, et al. Social functioning following pediatric stroke: contribution of neurobehavioral impairment.*Developmental neuropsychology.* 2018;43(4):312-328.

19. Lieb RW, Bohnert AM. Relations between executive functions, social impairment, and friendship quality on adjustment among high functioning youth with autism spectrum disorder. *Journal of autism and developmental disorders.* 2017;47(9):2861-2872.

20. Fong VC, Iarocci G. The Role of Executive Functioning in Predicting Social Competence in Children with and without Autism Spectrum Disorder.*Autism Research.* 2020;13(11):1856-1866.

21. Kirsch DG, Tarbell NJ. New technologies in radiation therapy for pediatric brain tumors: the rationale for proton radiation therapy.*Pediatric blood & cancer.* 2004;42(5):461-464.

22. Dinh JQ, Mahajan A, Palmer MB, Grosshans DR. Particle therapy for central nervous system tumors in pediatric and adult patients.*Translational Cancer Research.* 2012;1(3):137-149.

23. Hoffman KE, Yock TI. Radiation therapy for pediatric central nervous system tumors. *Journal of child neurology.* 2009;24(11):1387-1396.

24. Kahalley LS, Ris MD, Grosshans DR, et al. Comparing intelligence quotient change after treatment with proton versus photon radiation therapy for pediatric brain tumors. *Journal of Clinical Oncology.*2016;34(10):1043.

25. Kahalley LS, Peterson R, Ris MD, et al. Superior intellectual outcomes after proton radiotherapy compared with photon radiotherapy for pediatric medulloblastoma. *Journal of Clinical Oncology.*2020;38(5):454.

26. Gross JP, Powell S, Zelko F, et al. Improved neuropsychological outcomes following proton therapy relative to X-ray therapy for pediatric brain tumor patients. *Neuro-oncology.*2019;21(7):934-943.

27. Child AE, Warren EA, Grosshans DR, et al. Long-term cognitive and academic outcomes among pediatric brain tumor survivors treated with proton versus photon radiotherapy. *Pediatric Blood & Cancer.*2021:e29125.

28. Yock TI, Bhat S, Szymonifka J, et al. Quality of life outcomes in proton and photon treated pediatric brain tumor survivors.*Radiotherapy and Oncology.* 2014;113(1):89-94.

29. Conners CK, Pitkanen J, Rzepa SR. Conners 3rd Edition (Conners 3; Conners 2008). In: Kreutzer JS, DeLuca J, Caplan B, eds.*Encyclopedia of Clinical Neuropsychology.* New York, NY: Springer New York; 2011:675-678.

30. Altmann RA, Reynolds CR, Kamphaus RW, Vannest KJ. BASC-3. In: Kreutzer J, DeLuca J, Caplan B, eds. *Encyclopedia of Clinical Neuropsychology.* Cham: Springer International Publishing; 2017:1-7.

31. Salley CG, Gerhardt CA, Fairclough DL, et al. Social self-perception among pediatric brain tumor survivors compared with peers. *J Dev Behav Pediatr.* 2014;35(7):427-434.

32. Schulte F, Barrera M. Social competence in childhood brain tumor survivors: a comprehensive review. *Supportive Care in Cancer.*2010;18(12):1499-1513.

33. Barrera M SA, Speechley K, Maunsell E, Pogany L. Educational and Social Late Effects of Childhood Cancer and Related Clinical, Personal, and Familial Characteristics. *Cancer.* 2005(104):1751-1760.

34. Antonini TN, Ris MD, Grosshans DR, et al. Attention, processing speed, and executive functioning in pediatric brain tumor survivors treated with proton beam radiation therapy. *Radiotherapy and Oncology.* 2017;124(1):89-97.

35. Pulsifer MB, Sethi RV, Kuhlthau KA, MacDonald SM, Tarbell NJ, Yock TI. Early cognitive outcomes following proton radiation in pediatric patients with brain and central nervous system tumors.*International Journal of Radiation Oncology* Biology* Physics.*2015;93(2):400-407.

36. Yock TI, Yeap BY, Ebb DH, et al. Long-term toxic effects of proton radiotherapy for paediatric medulloblastoma: a phase 2 single-arm study.*The lancet oncology.* 2016;17(3):287-298.

37. Van Dyke J. The role of memory in language and communication. *Cognition and Acquired Language Disorders.* 2012:94-120.

38. Hanten G, Wilde EA, Menefee DS, et al. Correlates of social problem solving during the first year after traumatic brain injury in children. *Neuropsychology.* 2008;22(3):357.

39. Armstrong GT, Jain N, Liu W, et al. Region-specific radiotherapy and neuropsychological outcomes in adult survivors of childhood CNS malignancies. *Neuro-oncology.* 2010;12(11):1173-1186.

40. Poggi G, Liscio M, Galbiati S, et al. Brain tumors in children and adolescents: cognitive and psychological disorders at different ages. *Psycho-Oncology: Journal of the Psychological, Social and Behavioral Dimensions of Cancer.* 2005;14(5):386-395.

41. Baum KT, Powell SK, Jacobson LA, et al. Implementing guidelines: Proposed definitions of neuropsychology services in pediatric oncology. *Pediatric blood & cancer.* 2017;64(8):e26446.

42. Brodsky C, Shabason EK, Minturn JE, et al. Facial processing abilities and social functioning in pediatric brain tumor survivors, children with autism spectrum disorder, and typically developing children. In: American Society of Clinical Oncology; 2018.

43. Hocking MC, Parish-Morris J, Schultz RT, et al. Diminished social attention in pediatric brain tumor survivors: Using eye tracking technology during naturalistic social perception. *Neuropsychology.* 2020.

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