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Processing Speed in Children Treated for Brain Tumors: Effects of Radiation Therapy and Age

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Abstract

Objectives: The current study examined processing speed in children two years post-treatment for brain tumors (BT) with radiation therapy (RT) compared to those treated without RT.

Methods: Participants included 59 children (4–17 years) with BT assessed as part of the Brain Radiation Investigative Study Consortium (BRISC). Processing speed was assessed at two time points: T1 (3–9 months post-surgery) for 26 children who received whole brain or focal RT (RT group) and 33 treated without RT (no-RT group), and again two years later (T2) for 42 participants (17 RT, 25 no-RT). Linear mixed effects (LME) regression analyses examined differences in cognitive and motor speed between groups and across visits, with age at T1 (age1) treated as a moderating variable, and sex and primary tumor size as covariates.

Results: No effects for treatment group or visit were found for motor speed (Pegboard) or mean reaction time (Attention Network Task). On the Wechsler Processing Speed Index (PSI), the no-RT group performed better than the RT group, with a group-by-age interaction such that across visits, the difference between the no-RT and RT groups was larger among children who were older at initial treatment (> 10 years) than among those who were younger (<10 years).

Conclusions: Cumulative brain injury earlier in life (tumor, surgery, plus RT) may result in greater impact on more complex tasks of cognitive efficiency. Children receiving RT showed reduced processing speed over time, with a larger group difference among those who were over 10 years at treatment.

Keywords

neoplasms; child development; pediatric assessment; cancer; brain injury

Brain tumors are the most common neoplasm in children, with an annual age-adjusted incidence rate of 3.2 to 5.4/100,000 children (Ostrom et al., 2014; <https://nccd.cdc.gov/uscs/childhoodcancerbyprimarysite.aspx>). Recent advances in diagnosis and treatment have improved survival rates (Ward, DeSantis, Robbins, Kohler, & Jemal, 2014), but brain tumors (BT) and their treatment continue to convey notable morbidity. Treatment commonly includes resection, when possible, with adjunctive radiation or chemotherapy as required by tumor type and suspected malignancy. However, cognitive effects of resection, central nervous system (CNS)-directed radiation, and chemotherapy are common in childhood survivors (Mulhern, Merchant, Gajjar, Reddick, & Kun, 2004; Robinson et al., 2010), with CNS-directed radiation showing a dose-dependent impact over time (Grill et al., 1999; Kieffer-Renaux, Bulteau, Grill, Kalifa, Viguier, & Jambaque, 2000; Mitby et al., 2003).

Declines in functioning over time after BT treatment have been well documented (Gragert & Ris, 2011). These declines, or cognitive “late effects,” occur in intellectual ability (IQ), attention, and processing speed (Conklin et al., 2013; Kahalley et al., 2013; Palmer et al., 2001; Spiegler, Bouffet, Greenberg, Rutka, & Mabbott, 2004), which contribute to reduced functional outcomes (Armstrong, et al., 2009). Processing speed, in particular, is conceptualized as a “foundational capacity” supporting development of higher-level cognitive and other skills (Schatz, Kramer, Ablin, & Matthay, 2000). Due to its prolonged developmental course, processing speed may be more vulnerable to insult arising from BT and treatment (Armstrong, Blumberg, & Toledano, 1999). Processing speed is thought to be dependent on the integrity of white matter in the brain (Turken et al., 2008), which is impacted by surgical resection (Soelva et al., 2013) and is particularly sensitive to radiation (Reddick et al., 2005; Rueckriegel et al., 2010). Reductions in white matter have been linked to decreased processing speed in BT survivors (Aukema et al., 2009).

Outcomes for childhood BT survivors remain heterogeneous and evidence implicating resection and treatment on response speed remains inconsistent, and possibly dependent on the nature of the speeded response. For example, Spiegler and colleagues (Spiegler Bouffet, Greenberg, Rutka, & Mabbott, 2004) found no decline in children’s basic fine motor speed up to 6 years since BT treatment; however, lower intercepts at baseline assessment and a significant positive slope on the finger-tapping task suggested that acute effects of treatment on motor speed may resolve over time. De Ruiter and colleagues (de Ruiter, 2017) found reduced processing speed (indexed by Attention Network Task reaction time) in BT survivors relative to unaffected siblings, although treatment type was not associated with speed. In contrast, using a more cognitively complex measure (Wechsler Processing Speed Index [PSI] scores), others (Moxon-Emre, Bouffet, & Taylor, 2014), (Mabbott, et al., 2011) have found both lower performance at baseline assessment and declines in processing speed over time in children treated for BT. A recent meta-analytic review of BT survivors confirmed a large effect size for complex measures of processing speed (Robinson, Fraley, Pearson, Kuttisch, Compas, 2013).

Together, these findings suggest pediatric BT survivors show substantial reductions in speeded responding, although assessment timing may be an important moderating factor. Importantly, measurement of “processing” speed often conflates basic motor speed (e.g., fine finger dexterity) and reaction time with tasks requiring greater demands for response

selection and preparation or executive control, such as the Wechsler Processing Speed Index (PSI) (Jacobson et al., 2011). Thus, greater precision in examining the construct of processing speed may help to clarify understanding of outcomes in pediatric BT survivors.

Given the impact of treatment on long-term neurocognitive outcomes, interest is growing regarding factors that may moderate adverse effects. Risk factors for slower processing speed include treatment with (and dose/volume of) cranial radiation or chemotherapy (Kahalley et al., 2013; Kieffer-Renaux et al., 2000; Mabbott, Penkman, Witol, & Bouffet, 2008; Moxon-Emre et al., 2014) as well as age (Steinlin et al., 2003), tumor location (Beebe et al., 2005; Levisohn, Cronin-Golomb, & Schmahmann, 2000; Mabbott et al., 2011; Ris & Beebe, 2008), neurosurgery (Kahalley et al., 2013), presence of additional neurologic complications (Conklin et al., 2013; Mabbott, Penkman, Witol, & Bouffet, 2008; Moxon-Emre et al., 2014), and time since treatment (Mabbott et al., 2011; Moxon-Emre et al., 2014). Notably, these risk factors have not been consistently predictive across studies. While early work in this area found younger age at diagnosis to be predictive of greater decline—particularly among children treated with cranial radiation (Moore, Ater, & Copeland, 1992; Palmer et al., 2001)—more recent work suggests that age at diagnosis and/or treatment may not consistently moderate post-treatment processing speed (Kahalley et al., 2013; Konczak, Schoch, Dimitrova, Gizewski, & Timmann, 2005; Mabbott et al., 2011; Mabbott, Penkman, Witol, Bouffet, 2008). These findings may reflect recent improvements in treatment regimens designed to reduce morbidity for younger children (e.g., reductions in radiation dose, delayed radiation beyond age three years). Time since diagnosis also has inconsistently predicted post-treatment processing speed: some data show significant decline in children with an initial assessment close to treatment (Mabbott et al., 2011; Moxon-Emre et al., 2014), whereas others found minimal impact of time since treatment (Kahalley et al., 2013; Konczak, Schoch, Dimitrova, Gizewski, & Timmann, 2005; Mabbott, Penkman, Witol, Bouffet, 2008). Given this variability, additional data are needed to clarify the characteristics most predictive of post-treatment trajectories in processing speed.

Due to heterogeneity of samples across studies, identifying the most important moderators of neuropsychological outcomes has been challenging. The present study assessed stability of processing speed in children treated for BT, examining the role of cranial radiation and the potential effect of age at treatment. Specifically, we examined processing speed by assessing basic motor speed (e.g., pegboard task), choice reaction time on a computerized task, and the more cognitively demanding Wechsler PSI. We hypothesized that children treated with radiation would show poorer performance on all measures of processing speed compared to those treated without radiation, and that across treatment groups, those treated earlier in life, and those with larger lesions, would show the greatest reduction on speed-related tasks.

Methods

Participants

Participants included 59 children ages 4–17 years diagnosed with BT and treated at one of three centers: Cincinnati Children's Hospital Medical Center/Dayton Children's Hospital; Nationwide Children's Hospital; and Kennedy Krieger Institute/Johns Hopkins Hospital.

The children formed two groups: 1) the RT group completed whole brain or targeted 3D conformal radiation therapy or intensity modulated radiation therapy; 2) the no-RT group underwent resection only. The study was approved by IRBs at all participating institutions. Informed consent from the parent and child assent were obtained.

Children were excluded if they had severe developmental conditions (e.g., intellectual disability, autism spectrum disorder, etc.), severe morbidity related to surgery, sensory deficit that substantially limited participation, tumor recurrence requiring additional surgery or RT during the two-year study period, or malignant tumors (intrinsic brainstem glioma, glioblastoma multiforme) not expected to have progression-free survival for at least two years. Children with neurofibromatosis Type 1 were excluded because of primary involvement of white matter.

Participants were recruited from neuro-oncology clinics within the Departments of Hematology-Oncology and/or Neurosurgery at all sites. During the 4-year recruitment period, 420 potential participants undergoing neurosurgery for BT were screened. Of these, 307 did not meet eligibility criteria: 85 were too young, 64 were too old, 30 had severe pre-existing conditions/ineligible tumor types, 93 had severe post-surgical complications and were too ill to participate, 35 had NF1, and an additional 44 declined participation (e.g., family stress, lived out of state). Of the 69 participants that enrolled, 6 died before data collection and 4 dropped out, leaving a final sample of 59 patients with usable data at Time1. Seventeen additional participants dropped out between Time1 and Time2, leaving 42 patients with usable data at Time 2.

Design Considerations

The 4–17 year age range was selected to capture the median ages of diagnosis for the most common childhood BTs and to include those likely to be treated with RT. The sample was heterogeneous with regard to histology and location of tumor, age, and radiation dose and volume.

A no-RT comparison group controlled for pertinent factors affecting outcome, including general effects of tumor, neurosurgery, and impact of a life-threatening illness. Timing of the initial evaluation (T1) was chosen to allow for resolution of acute neurosurgical effects, but precede onset of delayed late-effects. Transient early late-effects are a possibility that must be considered (Armstrong et al., 2002), although our experience indicates that a window of relative stability occurs between 3 and 10 months post-surgery.

Procedures

Pediatric BT patients treated with RT commonly receive MRIs every 3–6 months for the first two years following RT, and every 9–12 months thereafter for at least five years. Collection of study neuropsychological data was timed to coincide as closely as possible with MRI scans. All neuropsychological and imaging data were collected starting 3–9 months post-surgery (± 1 month) for T1 visit.

Neuropsychological Assessment Strategy

The study emphasized the central role of processing speed, including measures of motor speed and reaction time. Neuropsychological assessment was completed at two points—Time1: (3–9 months post-surgery) and again two years later (± 2 months). Outcome variables included 1) PSI from WPPSI-3, WISC-IV, or WAIS-IV; 2) Purdue Pegboard (both hands trial) raw score total; and 3) mean reaction time from the Attention Network Task (ANT).

Processing Speed.—Processing speed was assessed using the Wechsler Intelligence Scale for Children-Fourth Edition (WISC-IV) (Wechsler, 2003) in children ages 6–16 years, the Wechsler Adult Intelligence Scale-Fourth Edition (WAIS-IV) (Wechsler, 2008) in participants who were age 17, and the Wechsler Preschool and Primary Scale of Intelligence-Third Edition (WPPSI-3) (Wechsler, 2002) in children under age 6 at the time of assessment. The PSI is the composite of two subtests (Symbol Search and Coding on each Wechsler scale).

Motor Speed.—Manual dexterity and fine motor speed were assessed using the Purdue Pegboard (Tiffin, 1968), which requires the child to place small pegs into holes aligned vertically in three 30-second conditions: first with the preferred hand, then the non-preferred hand, and then both hands simultaneously. The raw score represents the number of pegs correctly placed. The “both hands” trial was used as an outcome variable for the present study, to minimize the effects of handedness and maximize the demand on relevant white matter integrity, especially corpus callosum development (Roeder et al., 2008).

Reaction Time.—Reaction time was measured using the Attention Network Test (ANT) (Fan, McCandliss, Sommer, Raz, & Posner, 2002), a computerized vigilance task. For this task, a stimulus (picture of a fish) facing either left or right was presented in the middle of the computer screen. The child was required to press the right or left arrow key as quickly as possible, congruent with stimulus direction. Each stimulus was preceded by an alerting spatial cue that was congruent or incongruent with the anticipated location of the stimulus. The task involved three 7-minute sessions, with a short break in-between. The “Fish” version, described above, was administered to children 6–12 years. Participants ages 13–16 were given a version that substitutes arrows for the fish, but is otherwise identical in task demands. The mean reaction time for correct responses was used in analyses.

Radiation Therapy

Children in the RT group completed 3D conformal or intensity modulated radiation therapy; patient charts and radiotherapy treatment plans were reviewed to record gross treatment data. For supplemental exploratory analyses, type of radiation—focal vs. non-focal (i.e., cranial or craniospinal)—was used, to avoid conflating volume with dose.

Data Analyses

Socioeconomic status was estimated using the primary caregiver’s highest level of education. Age at assessment, caregiver education, size of primary lesion, and sex distribution between the RT and no-RT groups were compared using ANOVAs and chi-

square analyses. Linear mixed-effects models (LME) analyses with post-hoc Fisher's LSD test were used to examine group differences in the neuropsychological measures, using age at Time1 (age1), and visit (Time1 vs. Time2) as predictors, and sex and size of primary lesion as covariates. Exploratory analyses were conducted within the RT group to determine whether performance differed between patients receiving focal vs. non-focal RT. Given the relationship between disease factors and dropout rate, separate longitudinal analyses were also performed including only the 42 children who completed both assessments.

Results

Demographics

Demographics and test performance are listed in Tables 1 and 2. T1 data were available for 26 children in the RT group (22 boys) and 33 children in the no-RT group (19 boys). T2 data were available for 17 children in the RT group (14 boys) and 25 in the no-RT group (16 boys). At T1, groups did not differ in age [$F(1,57)=0.01$, $p=.757$], caregiver education [$F(1,57)=0.01$, $p=.927$], or primary lesion size [$F(1,56)=0.02$, $p=.879$]. They did differ in sex distribution at T1 [$\chi^2=5.02$, $p=.025$], with a greater proportion of boys in the RT group. At T2, the groups did not differ in age [$F(1,40)=0.08$, $p=.782$], caregiver education [$F(1,40)=0.01$, $p=.928$], primary lesion size [$F(1,39)=0.13$, $p=.719$], or sex distribution [$\chi^2=1.67$, $p=.300$]. Notably, participants who completed both visits did not differ significantly from those who dropped out on age [$F(1,57)=0.07$, $p=.789$], caregiver education [$F(1,57)=1.05$, $p=.310$], or primary lesion size [$F(1,56)=0.55$, $p=.462$]. Furthermore, although not all participants completed all measures at both time points, there were no differences between participants with and without complete data with regard to performance (Time1/Time2) on pegs ($t(51)=-.713$, $p=.479$ / $t(33)=-.120$, $p=.905$), ANT ($t(41)=-.543$, $p=.590$ / $t(31)=1.37$, $p=.173$), or PSI ($t(43)=-.590$, $p=.558$ / $t(39)=.174$, $p=.863$); age at Time 1 ($t(57)=-1.13$, $p=.264$), sex ($\chi^2_{(1)}=.232$, $p=.630$), or proportion above the median Family income ($\chi^2_{(1)}=.074$, $p=.786$) or education level ($\chi^2_{(1)}=.823$, $p=.364$).

Analyses of Processing Speed

PSI.—Initial LME analysis revealed a significant effect for group [$F(1,74)=7.07$, $p=.010$], such that across time, the RT group showed slower processing speed, compared to the no-RT group. The effects for visit [$F(1,74)=0.15$, $p=.697$], age at T1 (age1) [$F(1,74)=2.26$, $p=.137$], the group-by-visit [$F(1,74)=1.62$, $p=.208$] and group-by-visit-by-age1 interactions [$F(1,74)=1.72$, $p=.194$] were not significant. In contrast, the group-by-age1 interaction was significant [$F(1,74)=8.14$, $p=.006$]. Primary lesion size was not associated with PSI [$F(1,74)=1.55$, $p=.190$], and was dropped from remaining analyses.

The group-by-age1 interaction was explored by examining group differences in PSI across visits between children who were younger (<10 years) versus older (≥10 years). Age 10 years as selected as the split point for three reasons: first, it provided an essentially median split, allowing for fairly even groups in each subsample; second, it allowed for a roughly pre-post-pubertal split; and third, it has clinical significance in that children under 10 are elementary-aged while those over 10 are moving out of elementary school. Among younger children, across visits, sex was not associated with PSI ($p=.198$) and was dropped from the

model; however, in the older group sex was significantly associated with PSI ($p < .001$; girls out-performed boys) and was retained as a covariate. In the *younger* group, across visits, RT (88.7 ± 16.2) and no-RT (81.2 ± 13.5) groups did not differ in PSI [$F(1,36)=2.36$, $p=.134$, $\eta_p^2=.061$]. In contrast, within the *older* group, the RT group had lower PSI (81.9 ± 19.7) than the no-RT group (95.1 ± 15.5), with differences approaching significance [$F(1,45)=3.79$, $p=.058$, $\eta_p^2=.078$].

Across groups, children who completed both visits (88.3 ± 18.3) showed no significant differences in PSI at T1 compared to those who dropped out after T1 (80.1 ± 15.1) [$F(1,43)=2.13$, $p=.152$, $\eta_p^2=.047$]. However, group moderated the relationship between T1 performance and dropout. Within the RT group, children who dropped out exhibited lower PSI at T1 (71.6 ± 12.5) than those completing both visits (91.1 ± 21.3) [$F(1,16)=4.76$, $p=.044$, $\eta_p^2=.229$]. In contrast, in the no-RT group, T1 PSI did not differ between those who dropped out (88.7 ± 12.83) and those who did not (86.8 ± 16.7) [$F(1,25)=0.08$, $p=.781$, $\eta_p^2=.003$].

Given the potential for disease-related factors to influence dropout and bias subsequent results, we conducted identical supplementary analyses including *only* children completing both T1 and T2 assessments ($n = 42$; Figure 2). This subsample showed a nearly identical pattern of results, with significant effects for group (no-RT > RT) [$F(1,63)=7.49$, $p=.008$] and the group-by-age1 interaction [$F(1,63)=7.23$, $p=.009$], but no significant differences for visit, group-by-visit, or group-by-visit-by-age1 interactions. Among children in the RT group completing both visits ($n = 11$), there were no PSI differences by treatment type (focal vs. non-focal RT) at T1 [$F(1,9)=0.02$, $p=.900$, $\eta_p^2=.002$].

Together, findings highlight higher better overall PSI performance in the no-RT group compared to the RT group, across visits, with findings dependent on age at baseline, such that older children demonstrated a larger between-group performance difference. Neither size of lesion nor type of RT (among those receiving RT) was associated with PSI.

Purdue Pegboard.—Initial LME analysis revealed a significant effect for age1 on Pegboard performance [$F(1,77)=25.4$, $p < .001$], as expected, given that the Pegboard score is not standardized by age. Conversely, there were no significant effects for group [$F(1,77)=0.01$, $p=.964$], visit [$F(1,77)=0.12$, $p=.778$], and no significant 2- or 3-way interactions ($p \geq .50$ for all). Size of primary lesion was associated with lower performance across groups and visits [$F(1,77)=9.19$, $p=.003$]. Within the RT group, performance did not differ by treatment type (focal vs. non-focal) at T1 [$F(1,23)=.41$, $p=.528$, $\eta_p^2=.019$] or T2 [$F(1,13)=3.27$, $p=.094$, $\eta_p^2=.201$], although at T2, those receiving focal RT (10.0 ± 1.4) outperformed those with non-focal (7.6 ± 2.8) RT. At T1, no differences were found in Pegboard performance between children who completed both visits (7.2 ± 3.3) and those dropping out (6.9 ± 3.6) [$F(1,51)=0.48$, $p=.827$, $\eta_p^2=.001$].

Re-analysis of the full LME using only those participants who completed both visits yielded nearly identical findings, such that there was a significant effect for age1 on Pegboard performance ($p < .001$), but not for group ($p = .969$), visit ($p=.442$), or any of the 2- or 3-way

interactions (all $p > .500$). Within the RT group ($n = 15$), no performance differences were found between those receiving focal vs. non-focal RT [$F(1,14) = 0.99$, $p = .339$, $\eta_p^2 = .070$].

ANT Mean Reaction Time.—Initial LME analysis revealed a significant effect for age1 on ANT reaction time [$F(1,64) = 20.7$, $p < .001$], as expected, given that this score is not standardized for age. Conversely, there were no significant group [$F(1,64) = .41$, $p = .523$], visit [$F(1,64) = 0.01$, $p = .911$], or 2- or 3-way interactions ($p > .25$ for all). Size of primary lesion was not significantly associated with ANT performance across groups and visits [$F(1,64) = 2.01$, $p = .153$].

Within the RT group, those receiving focal vs. non-focal RT did not differ in ANT mean reaction time at T1 [$F(1,17) = .20$, $p = .174$, $\eta_p^2 = .106$] or T2 [$F(1,12) = 3.64$, $p = .081$, $\eta_p^2 = .233$]. At T1, no differences in ANT reaction time were found between children who completed both visits and those who dropped out [$F(1,41) = 0.01$, $p = .938$, $\eta_p^2 < .001$].

Re-analysis of the full LME using only those participants who completed both visits yielded nearly identical findings, with a significant effect for age1 ($p < .001$), but no effect for group ($p = .602$), visit ($p = .368$), or any 2- or 3-way interactions (all $p > .33$). Within the RT group ($n = 11$), no differences were found in baseline ANT reaction time between those receiving focal vs. non-focal RT [$F(1,9) = 0.01$, $p = .996$, $\eta_p^2 < .001$].

Discussion

The study examined the effect of RT on multiple tasks assessing processing speed in children treated for BT, specifically investigating the impact of age at treatment. When measuring processing speed using basic motor speed and reaction time, no significant differences were observed between the RT and no-RT groups initially or over time. For PSI, in contrast, the RT group performed more poorly than the no-RT group, with children who were older at time of treatment showing a larger group difference than those treated at younger ages. These findings suggest that radiation effects on processing speed in children may differ, depending on the level of higher cognitive demand inherent in the tasks. For example, the PSI tasks involve visual reprocessing, mental transformation, and associative memory (Jacobson et al., 2011), as contrasted with less complex tasks requiring basic motor speed or reaction time. These data also highlight moderating effects on differences in PSI scores by age.

Our pattern of findings contrast with prior research in this area, although differences in assessment of the effects of age and duration of follow-up may explain some of the disparate findings. For example, in examining trajectories of motor skill in children treated for BT, Spiegler and colleagues (Spiegler, Bouffet, Greenberg, Rutka, & Mabbott, 2004) found an initial reduction (lower intercept) in simple motor speed after treatment, but a positive slope, suggesting the adverse acute impact of tumor and treatment lessened over time; whereas a separate longitudinal examination of speed in children treated for BT showed initial reduction in performance (lower intercept), *plus* a pattern of decline over time, although degree of decline appeared dependent upon supratentorial tumor location (Mabbott et al., 2011). Moxon-Emre et al. (Moxon-Emre et al., 2014) also found lower performance at

baseline *and* declines in PSI over time in BT survivors, and Palmer et al. (Palmer et al., 2013) also found impacts on processing speed intercept and slope. Notably, in the Palmer et al. sample, older children showed lower baseline speed but greater stability than younger children, and younger age was associated with reduced speed over time (particularly for children with high risk disease).

Drawing definitive conclusions is complicated by the fact that differences in outcomes among studies may reflect differences in tumor types (i.e., our sample was heterogeneous with regard to tumor type), timing of “baseline” assessment relative to diagnosis, follow-up interval, and age. Initial assessment in the present study took place three to nine months after resection, close to diagnosis but perhaps after acute impacts of resection were resolved, whereas other studies have completed “baseline” assessment at one year (Palmer et al., 2013) and up to 15 years (Spiegler, Bouffet, Greenberg, Rutka, & Mabbott, 2004) after treatment. Furthermore, our follow-up interval was shorter than that of several of the studies described earlier, which followed patients for five years and beyond. Finally, the mean age of participants has varied substantially across samples; the mean age of participants in Spiegler et al. (Spiegler, Bouffet, Greenberg, Rutka, & Mabbott, 2004) was much younger (i.e., 6.08 years) than that of our sample, Palmer et al. (Palmer et al., 2013) (9.82), or Mabbott et al. (Mabbott et al., 2011) (11.66). Few studies have specifically considered the potential effects of age at treatment on speeded output; our findings add to the understanding of those factors likely to impact children’s outcomes over time after BT treatment.

Limitations

Several factors limit interpretation of findings. Substantial attrition occurred between time points, such that almost one-third of the sample did not complete the second assessment. Attrition resulted in uneven groups for examination of specific impacts of RT type, limiting our ability to consider how this factor affects results. While Pegboard performance and ANT reaction time did not differ between those who dropped out versus those who persisted, PSI scores at T1 were lower among RT group participants who dropped out compared to those who completed the T2 visit, suggesting that more impaired participants dropped out and highlighting the potential for disease-related factors to have influenced our ability to track outcomes over time. Sex distribution was uneven between groups, limiting consideration of sex as a moderator. Finally, results may have been confounded by tumor location, given the relatively greater percentage of non-infratentorial tumors in the no-RT group. Along with tumor location, subgroup sizes in the current sample were too small to permit valid examination of effects to tumor lateralization and future work in larger samples should examine effects of tumor lateralization on performance of processing speed tasks.

Nevertheless, the prospective longitudinal approach is a strength of the study, and given the overall rarity of childhood cancer and the importance of a more nuanced examination of processing speed, the current findings provide important evidence that changes in processing speed during the more immediate post-treatment period are impacted by age at treatment. More specifically, the effects of RT as a treatment for childhood BT may be most evident in speeded tasks requiring greater cognitive involvement.

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Figure 1.
Mean Group Processing Speed Index by Visit (All Participants)

Figure 2.
Mean Group Processing Speed Index by Visit (Only Participants Completing Both Visits; $n = 42$)

Table 1.

Means of Demographic Variables for Radiation and no-Radiation Groups

	No-RT (n = 33)	RT (n = 26)
Type of Tumor	Astrocytoma (14) Craniopharyngioma (2) Choroid Plexus (2) Ganglioglioma (2) Other (13; glioma, meningioma, DNET, SEGA)	Medulloblastoma/PNET (12) Germ cell (3) Ependymoma (3) Astrocytoma (2) Other (8; optic nerve glioma, germinoma, ATRT)
Tumor Location ($\chi^2_{(1)}=5.76, p=.016$)	Infratentorial (10) Supratentorial (23)	Infratentorial (16) Supratentorial (10)
Received Chemotherapy	4	19
Type of Chemotherapy	Vincristine (4) Platinum (4)	Vincristine (16) Platinum (16) Both agents (14); Other (1)
Radiation	N/A	Focal (9) Cranial/Craniospinal (17) % dose under 24 Gy=42.3
Annual Household Income [^] ($\chi^2_{(1)}=.179, p=.672$)	Median =11.0 Range=1–15 % above Median =48.0	Median=12.0 Range=2–15 % above Median=42.4
Caregiver Education [*] ($\chi^2_{(1)}=.081, p=.776$)	Median =14.0 Range=10–16 % above Median=30.3	Median =14.0 Range=10–16 % above Median=26.9
Sex (Percent Male) ($\chi^2_{(1)}=5.02, p=.025$)	57.6	84.6

Note.

[^] According to the following scale: 1=Less than or equal to \$3,000; 2=\$3,001-\$6,000; 3=\$6,001-\$9,000; 4=\$9,001-\$12,000; 5=\$12,001-\$15,000; 6=\$15,001-\$20,000; 7=\$20,001-\$30,000; 8=\$30,001-\$40,000; 9=\$40,001-\$50,000; 10=\$50,001-\$60,000; 11=\$60,001-\$70,000; 12=\$70,001-\$80,000; 13=\$80,001-\$90,000; 14=\$90,001-\$100,000; 15= Over \$100,000.

^{*} According to the following scale: 10=10th; 11=11th; 12=12th; 13=Partial college/technical/business; 14=College graduate; 15=Partial graduate school; 16=Graduate degree

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Note: SES = Primary caregiver highest level of education; lesion = size of primary lesion (mm²); PSI = Processing Speed Index (WISC-IV/WPPSI-3/WAIS-IV); PP = Purdue Pegboard (both hands trial) raw score; ANT = Attention Network Task mean reaction time (msec).