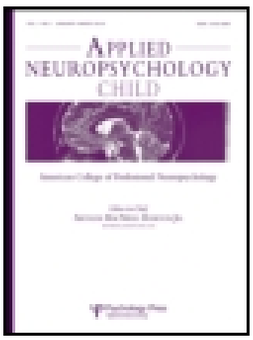

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Working memory training in pediatric brain tumor survivors after recent diagnosis: Challenges and initial effects

Rachel E. Siciliano[a], Jennifer C. Thigpen[a], Leandra Desjardins[a], Jessica L. Cook[a], Ellen H. Steele[a], Meredith A. Gruhn[a], Megan Ichinose[b], Sohee Park[b], Adam J. Esbenshade[c], Devang Pastakia[c], John C. Wellons[d], and Bruce E. Compas[a]

[a]Department of Psychology and Human Development, Vanderbilt University, Nashville, Tennessee, USA; [b]Department of Psychology, Vanderbilt University, Nashville, Tennessee, USA; [c]Department of Pediatrics, Vanderbilt University Medical Center, Nashville, Tennessee, USA; [d]Department of Neurosurgery, Vanderbilt University Medical Center, Nashville, Tennessee, USA

ABSTRACT

Research shows promise for cognitive interventions for children diagnosed with brain tumors. Interventions have been delivered approximately 5 years postdiagnosis on average, yet recent evidence shows cognitive deficits may appear near diagnosis. The present study assessed the feasibility and initial effects of working memory training in children with brain tumors delivered soon after diagnosis and followed 2 years postdiagnosis. Children completed baseline assessments 10 months postdiagnosis and were randomized to complete adaptive or nonadaptive (i.e., control) Cogmed Working Memory Training. Children were administered the WISC-IV Working Memory Index (WMI) and NIH Toolbox Cognitive Battery (NTCB), and parents completed attentional and executive function measures at four time points. On average, participants completed half of prescribed Cogmed sessions. Retention for the three follow-up assessments proved difficult. For both Cogmed groups, WMI and NTCB scores significantly improved immediately postintervention compared to baseline scores. Significant differences were not maintained at the remaining follow-ups. There was preliminary evidence for improved executive function at the final follow-up on parent-reported measures. Working memory training closer to diagnosis proved difficult, though results suggest evidence of cognitive improvement. Future studies should continue to examine potentially efficacious interventions for children with brain tumors and optimal delivery windows to maximize impact.

KEYWORDS

Brain tumor; cancer; cognition; intervention; pediatric; working memory

Introduction

Brain and central nervous system tumors are the most common solid tumor and the second leading cause of cancer death in individuals 0–19 years of age (Siegel et al., 2020). While significant advances in the identification and treatment of pediatric brain tumors have led to demonstrable increases in survival rates for children and adolescents (Ostrom et al., 2016), pediatric brain tumor survivors continue to experience adverse effects on cognitive function (Iuvone et al., 2011; Robinson et al., 2010). Recent evidence indicates that cognitive problems are affected by both characteristics of tumors themselves as well as treatment (Fraley et al., 2019; Robinson et al., 2010). The majority of research has focused on late effects during survivorship, typically several years after diagnosis and after treatment has ended (Robinson et al., 2010, 2013; Tonning Olsson et al., 2014). However, recent research suggests that deficits can appear prior to surgery (Fraley et al., 2019; Thigpen et al., 2016). The identification of cognitive deficits presurgically raises the possibility that it may be beneficial for interventions to be delivered near diagnosis or during adjuvant treatment (i.e., radiation and/or chemotherapy) to remediate deficits or prevent further decline (Coomans et al., 2019). The current study was designed to investigate the feasibility, acceptability, and initial proof of concept of a working memory training program offered to children with brain tumors shortly after their initial diagnosis.

Primary aspects of cognitive function that are affected in children with brain tumors are executive function, including working memory (Araujo et al., 2017; Conklin et al., 2012; Kirschen et al., 2008; see Mabbott et al., 2008 for an exception). Working memory is essential for processing, managing, and storing new information for complex cognitive tasks including learning, reasoning, and comprehension, and may be particularly affected by cancer treatments (Law et al., 2011). Both parent-reported and working memory performance scores measured immediately postsurgery have been shown to significantly decreased over time in children with brain tumors (Duda et al., 2020; Knight et al., 2014; Palmer et al., 2013). Therefore, interventions to improve working memory or prevent cognitive decline are a high priority.

CONTACT Bruce E. Compas bruce.compas@vanderbilt.edu Department of Psychology and Human Development, Vanderbilt University, Nashville, TN 37232, USA.

Current options for interventions targeting impairment in pediatric brain tumor patients and survivors include use of stimulant medications for difficulties in attention (Conklin et al., 2007, 2010), in-person cognitive remediation programs (Butler et al., 2008; Patel et al., 2009), and computer-based cognitive-remediation programs that can be delivered at home or in the hospital (Conklin et al., 2017; Hardy et al., 2013). Stimulant medications have been investigated in pediatric cancer survivors yet may not be optimal for some due to side effects (Conklin et al., 2007, 2009, 2010). While in-person, clinic-based interventions are potentially efficacious, participation, adherence, and cost present challenges for implementation (Butler et al., 2008; Patel et al., 2009). Computerized at-home working memory training has the appeal of minimal risk and greater convenience for families. Studies of computerized working memory training in pediatric brain tumor survivors have shown that it is feasible and acceptable for families when administered several years after diagnosis (Carlson-Green et al., 2017; Cox et al., 2015; Hocking et al., 2019). However, findings have been mixed for the efficacy and impact on near and far transfer in pediatric cancer populations (Conklin et al., 2015, 2017; Cox et al., 2015; Hardy et al., 2013). Of note, working memory training interventions in pediatric brain tumor survivors have been delivered an average of 5 years post-treatment completion (Carlson-Green et al., 2017; Conklin et al., 2015; Cox et al., 2015; Hardy et al., 2013). Researchers have yet to investigate if computerized at-home training is feasible when delivered earlier in the course of brain tumor treatment and recovery or prior to the onset of late effects.

The present study examined the feasibility and acceptability of cognitive intervention in children with newly diagnosed brain tumors delivered shortly postdiagnosis and estimate the initial effects on outcomes over the course of 2 years postdiagnosis. We provided a rigorous test of a cognitive intervention by comparing an adaptive version of the Cogmed program (http://www.cogmed.com) to an active control condition using a nonadaptive version of the program. We hypothesized that (1) pediatric brain tumor patients would utilize the Cogmed working memory training program at an acceptable rate as defined by at least 85% of the program sessions over the 5-week training period; and (2) as reflected in a group × time interaction, participants randomized to the adaptive Cogmed group would show greater improvement on measures of working memory and executive function at postintervention follow-up assessments as compared to those assigned to the nonadaptive Cogmed group.

Methods

Participants

Over the course of 3 years of recruitment, 49 patients were identified as eligible and consented to the study at a university-affiliated children's hospital in the southeastern U.S. All patients identified by the pediatric neurosurgery team aged 7–16 years with a first diagnosis (i.e., not a recurrence) of primary brain tumor who could complete assessment and study activities in English were eligible. Participants were not eligible if they had a preexisting neurodevelopmental disorder or disability (e.g., intellectual disability), pervasive developmental disorder (e.g., autism), or a diagnosis of neurofibromatosis because illness and treatment course is significantly different from other children with central nervous system tumors. All parents who were approached by the medical team indicated they would be willing to learn more about the study from a member of the research team. Eight consented participants did not complete cognitive measures at any time point ($n = 3$) or the preintervention assessment ($n = 5$). Therefore, the final sample included 41 pediatric brain tumor patients (84% of those eligible). Children were approximately 12 years on average, 61% were male, 29% underwent surgery only, and 71% underwent both surgery and adjuvant treatment (i.e., chemotherapy, radiation). Participant characteristics are reported in Table 1.

Measures

Cognitive functioning

General intellectual functioning was assessed preintervention using the Wechsler Abbreviated Scales of Intelligence, Second Edition (WASI-II; Wechsler, 2011), two subtest Full Scale IQ estimate. At each time point, participants completed the Wechsler Intelligence Scale for Children, Fourth Edition (WISC-IV; Wechsler, 2003) Working Memory Index (WMI), including Digit Span and Letter Number Sequencing subtests.

Participants also completed five subtests of the National Institutes of Health Toolbox Cognition Battery (NTCB), including the Dimensional Change Card Sort Test (cognitive flexibility and attention measure), Flanker Inhibitory Control and Attention Test (executive function and inhibitory control measure), List Sorting Working Memory Test (working memory measure), Pattern Comparison Processing Speed Test (processing speed measure), Picture Sequence Memory Test (episodic memory measure), which together yield a Fluid Cognition Composite. The NTCB is a brief, standardized, computerized neuropsychological battery for children with well-established validity and reliability, designed to control for practice effects (Bauer & Zelazo, 2013, 2014; Gershon et al., 2013).

Executive function and attention

Parents reported their child's executive functioning on the Behavior Rating Inventory of Executive Function (BRIEF), a parent rating scale of behavioral aspects of cognitive functions, which has demonstrated good validity across multiple populations (Gioia et al., 2000, 2008). Parents completed the Child Behavior Checklist (CBCL), a measure with well-established reliability and validity (Achenbach & Rescorla, 2001). The Attention Problems Scale from this measure was used.

Table 1. Demographic and treatment information for randomized participants.

	Full sample ($n = 41$)		Adaptive ($n = 20$)		Nonadaptive ($n = 21$)		Group comparison
	M (SD)	*N* (%)	*M* (SD)	*N* (%)	*M* (SD)	*N* (%)	*t* (*p*)
Age (years)	11.98 (2.68)	—	12.31 (2.57)	—	11.67 (2.81)	—	0.77 (0.45)
Gender							0.50 (0.62)
Male	—	25 (61)	—	13 (65)	—	12 (57)	
Female	—	16 (39)	—	7 (35)	—	9 (43)	
Tumor type[a]	—				—		0.16 (0.87)
Low grade	—	20 (49)	—	10 (50)	—	10 (48)	
High grade	—	19 (46)	—	9 (45)	—	11 (52)	
Treatment type[b]	—		—		—		0.57 (0.57)
Surgery only	—	12 (29)	—	5 (25)	—	7 (33)	
Surgery + adjuvant	—	29 (71)	—	15 (75)	—	14 (67)	
Months since surgery[3]	10.38 (15.38)	—	12.11 (16.97)	–	8.72 (13.92)	—	0.70 (0.49)
FSIQ	99.29 (12.29)	—	100.60 (13.87)	–	98.05 (10.77)	—	0.66 (0.51)

All participants who completed the preintervention (T1) assessment. Group comparison reflects independent samples *t*-test values. Adjuvant = chemotherapy and/or radiation; FSIQ: pre-intervention full scale IQ as measured by the WASI.
[a]Tumor type information was missing for two participants (one from each Cogmed group); data reflect $n = 39$.
[b]All participants (100% of our sample) underwent neurosurgery.
[c]Months since surgery reflects the average time between surgery and the T1 preintervention assessment.

Procedure

The pediatric neurosurgery and neuro-oncology teams consecutively identified eligible newly diagnosed brain tumor patients ages 7 and 16-years-old at a university-affiliated children's hospital. A pediatric neurosurgeon or oncologist introduced the study and asked if families were interested in being contacted by the research team. If a parent indicated interest, the medical provider supplied parent contact information to the study coordinator within 24 h of diagnosis, who then contacted the parent via phone or in person in the hospital. If both the parent and child were interested, written consent was obtained from parents and assent from children. Assessments were completed in the hospital or nearby research space. The preintervention (T1) baseline assessment was planned to be conducted at 10–20 weeks postdiagnosis, the postintervention (T2) assessment at 5–8 weeks after completion of the Cogmed program, the next follow-up (T3) 10–20 weeks postintervention, and the final follow-up (T4) 6 months after the previous assessment.

Cognitive training protocol

The commercially available Cogmed software package (http://www.cogmed.com) was utilized. Cogmed has support for its efficacy in clinical trials and has a version specifically designed for children and adolescents (Gray et al., 2012; Hardy et al., 2013). Two versions of the Cogmed program were used: the *adaptive* version, which adjusts to daily performance by tailoring activities by getting more or less difficult based on participant performance, and the *nonadaptive* version, which does not adjust activity difficulty and remains at the same difficulty level across all training sessions. The computer-based Cogmed training program consists of tasks designed to engage working memory, processing speed, and attention skills that encompass aspects of executive function. After completion of the T1 assessment, participants were block randomized to receive either the adaptive or nonadaptive version of Cogmed by type of tumor treatment received (i.e., surgery only, surgery + adjuvant care). Participants were naive to their group assignment and asked to complete program sessions lasting from 30 to 45 min, 5 days per week over a 5-week period for a total of 25 sessions. Trained coaches provided supportive contact by phone, text message, and email one to two times per week.

Statistical power and data analyses

Statistical analyses were conducted with the Statistical Package for Social Sciences (SPSS) version 25. Means and standard deviations were calculated for demographics and variables of interest. Independent samples *t*-tests were conducted for group comparisons on participant characteristics. We conducted repeated measures ANOVAs to analyze differences in working memory and executive function over time by Cogmed group assignment (adaptive vs. nonadaptive) and we tested group × time interactions to determine if changes in cognitive function across time varied as a function of Cogmed group assignment. Analyses were corrected for multiple comparisons using the Bonferroni method. Power analyses indicated that with $N = 41$ (adaptive $n = 20$, nonadaptive $n = 21$), $\alpha = .05$, and $1 - \beta = .80$, large effects could be detected for independent samples *t*-tests ($d > .90$), and medium to large effects for repeated measures ANOVA F tests ($f > .40$), and linear multiple regressions ($f^2 > .33$). All tests were two-tailed. Effect sizes were interpreted using Cohen's (1988) guidelines.

Results

Participant enrollment and retention

Randomization was successful, as participants in the adaptive and nonadaptive Cogmed groups did not differ based on sex, age, tumor grade, treatment type, time since diagnosis, nor pre-intervention baseline FSIQ (Table 1). Assessments were not completed within the specified study goals for T1 (see Table 2). The study goal for T3 was met, while the T4 assessment was not. Participants completed

Table 2. Participant enrollment, retention, and Cogmed completion.

	Goal	Actual
Assessment completion		
T1 Assessment	2.5−5 months postsurgery	10.4 months postsurgery
T2 Assessment	5−8 weeks postintervention	9.1 weeks postintervention
T3 Assessment	10−20 weeks postintervention	14.5 weeks postintervention
T4 Assessment	6 months from T3	9.9 months from T3
Cogmed completion		
Within 5 weeks	85%	24%
Prior to T2	85%	32%
Sessions completed	Number of sessions	Percentage of prescribed sessions
Within 5 weeks	13	52%
Prior to T2	16	64%

Table 3. Assessment completion over time by group.

	Full sample *N* (%)	Adaptive *N* (%)	Nonadaptive *N* (%)	Group comparison *t* (*p*)
T1	41 (100)	20 (100)	21 (100)	–
T2	26 (63)	9 (45)	17 (81)	2.50 (0.02)*
T3	33 (80)	16 (80)	17 (81)	0.08 (0.94)
T4	26 (63)	12 (60)	14 (67)	0.76 (0.45)

T1: preintervention assessment; T2: postintervention assessment; T3: 10–20 weeks postintervention; T4: final follow-up 6 months after the previous assessment.
*$p < .05$.

three of the four assessments on average ($M = 3.51$, SD = 1.03). The number of assessments completed did not vary by Cogmed group or treatment type. Of the 41 participants, 26 completed the post-intervention T2 assessment, which varied by group, $t(39) = 2.50$, $p = .02$, with more participants randomized to the nonadaptive Cogmed program completing the T2 assessment than those randomized to adaptive Cogmed (Table 3). The T3 and T4 assessment completion did not vary by group.

Time since diagnosis was not correlated with WMI scores at any time point, nor with NTCB Fluid Cognition Composite at T2, T3, or T4. However, at T1, children assessed farther from diagnosis had lower NTCB Fluid Cognition Composite scores ($r = -.39$, $p = .02$), therefore the time between diagnosis and T1 was included as a covariate.

Feasibility and acceptability of working memory training

The first hypothesis (i.e., 85% completion of prescribed sessions) was not supported; 10 of the 41 participants met this threshold within the prescribed 5 weeks, and 13 of the 41 participants completed 85% prior to completing their T2 assessment. Across all participants, a mean of 13 sessions were completed during the 5 weeks, with an additional three sessions completed outside of the prescribed 5 weeks for a mean of 16 sessions completed prior to the T2 assessment. The number of sessions completed in 5 weeks did not vary by group, nor did the total number completed. Linear regressions showed that child age, baseline Full Scale IQ, baseline WMI, BRIEF Global Executive Composite, and CBCL Attention Problems Scale scores did not predict the number of Cogmed sessions completed ($p > .05$). The number of sessions also did not vary based on treatment type (i.e., surgery only vs. surgery + adjuvant).

Executive function between groups across discrete time points

There was significant participant dropout, particularly for the adaptive group. Therefore, to maximize the available sample size and increase power to detect possible differences on key cognitive variables, we conducted separate repeated measures ANOVAs examining the effects of group and time from T1 to T2, T1 to T3, and T1 to T4 on WISC-IV WMI and NTCB Fluid Cognition Composite scores, covarying for time since diagnosis (see Table 4). From T1 to T2, there was a significant effect of time on WMI scores, $F(1, 22) = 6.53$, $p = .02$, $\eta^2 = .23$, with higher scores at T2. The group X time interaction approached significance, $F(1,22) = 3.78$, $p = .07$, $\eta^2 = .15$ and is shown in Figure 1. There was a trend for a greater increase in WMI scores from T1 to T2 for children in the adaptive group. The time effect was not maintained from T1 to T3 or T1 to T4, and group × time interactions were not significant ($p > .05$).

From T1 to T2, there was a significant effect of time on NTCB Fluid Cognition Composite scores, $F(1, 17) = 8.75$, $p = .009$, $\eta^2 = .34$ (Figure 1). From T1 to T3, there was a significant time effect for NTCB scores, $F(1, 22) = 10.37$, $p = .004$, $\eta^2 = .32$. From T1 to T4, time remained a significant predictor of NTCB scores, $F(1,17) = 8.45$, $p = .01$, $\eta^2 = .33$. All time effects were in the predicted direction, with higher scores postintervention (Table 4). Group × time interactions were not significant ($p > .05$).

Executive function between groups across all time points

To supplement discrete time point analyses, we conducted repeated measures ANOVAs examining Cogmed group as a between-subjects factor, and time as a within-subjects factor. Time between diagnosis and T1 assessment was included as a covariate. Results showed a similar pattern to analyses of discrete time points. There was a significant main effect of time, $F(3, 42) = 2.95$, $p = .04$, $\eta^2 = .17$ (see Figure 2). Post hoc pairwise comparisons demonstrated that postintervention T2 WMI scores were significantly higher than T1 scores, $p = .04$. This difference was no longer significant at

Table 4. Pre- and post-intervention cognitive and executive function measures by Cogmed group with maximized samples from discrete time points.

		Full sample M (SD)	Adaptive M (SD)	Nonadaptive M (SD)	Group comparison *F* (*p*)
WMI					
T1–T2 Model[a]	T1	96.68 (11.10)	89.88 (12.63)	99.88 (9.00)	2.62 (.12)
	T2	100.88 (12.05)	98.75 (15.87)	101.88 (10.20)	
T1–T3 Model [b]	T1	93.83 (11.71)	90.87 (12.00)	96.80 (11.01)	1.63 (.21)
	T3	97.27 (14.80)	94.40 (13.14)	100.13 (16.23)	
T1–T4 Model[c]	T1	92.32 (11.96)	87.00 (11.76)	95.87 (11.08)	1.86 (0.19)
	T4	93.36 (20.67)	88.30 (18.22)	96.73 (22.11)	
NTCB					
T1–T2 Model[d]	T1	90.62 (14.25)	92.26 (15.52)	89.74 (14.10)	0.04 (0.85)
	T2	97.49 (18.96)	97.99 (18.56)	97.22 (19.93)	
T1–T3 Model[e]	T1	91.31 (15.82)	92.89 (17.47)	89.61 (14.39)	0.00 (0.97)
	T3	100.45 (20.05)	99.00 (21.45)	102.01 (1924)	
T1–T4 Model[f]	T1	88.76 (15.35)	87.10 (15.58)	90.41 (15.76)	0.53 (0.47)
	T4	99.48 (19.08)	95.04 (17.21)	103.92 (20.70)	

NTCB: NIH Toolbox Cognition Battery Fluid Cognition Composite; T1: preintervention assessment; T2: postintervention assessment; T3: 10–20 weeks postintervention; T4: final follow-up 6 months after the previous assessment; WMI: Wechsler Intelligence Scales Working Memory Index.
[a]$n_{total} = 25$; $n_{adaptive} = 8$; $n_{nonadaptive} = 17$; [b]$n_{total} = 30$; $n_{adaptive} = 15$; $n_{nonadaptive} = 15$; [c]$n_{total} = 25$; $n_{adaptive} = 10$; $n_{nonadaptive} = 15$; [d]$n_{total} = 20$; $n_{adaptive} = 7$; $n_{nonadaptive} = 13$; [e]$n_{total} = 25$; $n_{adaptive} = 13$; $n_{nonadaptive} = 12$; [f]$n_{total} = 20$; $n_{adaptive} = 10$; $n_{nonadaptive} = 10$.
*$p < .05$.

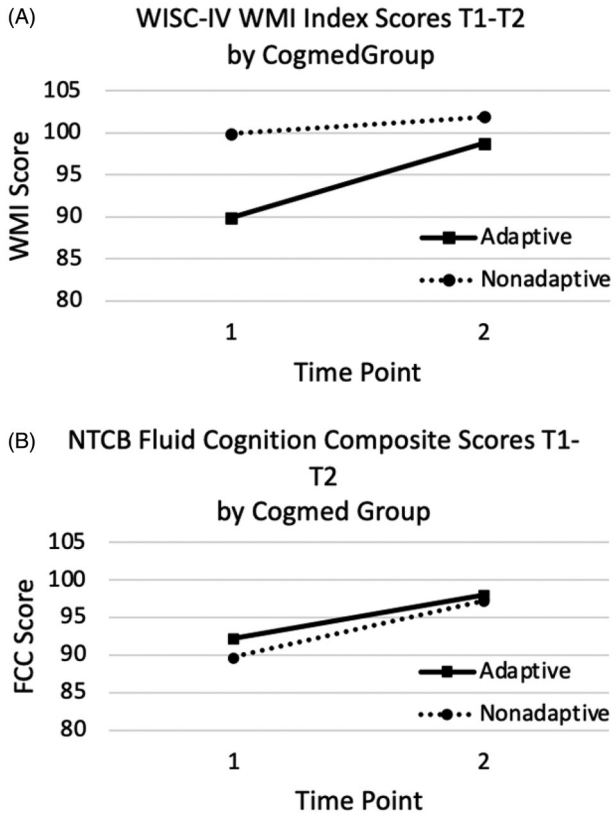

Figure 1. Repeated measures ANOVAs of WISC-IV Working Memory Index (A) and NTCB fluid cognition composite (B) Scores Preintervention (T1) to immediately postintervention (T2) by Cogmed group.

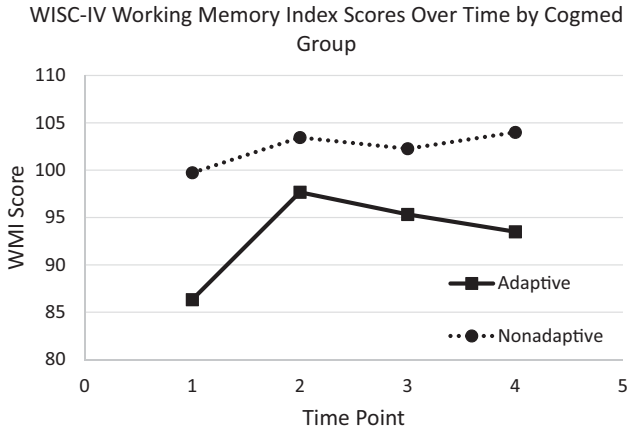

Figure 2. Repeated measures ANOVA of WISC-IV Working Memory Index Scores across all time points by Cogmed group.

Table 5. Pre and postintervention cognitive and executive function measures by Cogmed group across all time points.

	Full sample *M* (SD)	Adaptive *M* (SD)	Nonadaptive *M* (SD)	Group comparison *t* (*p*)
WMI				
T1	95.00 (11.61)	86.33 (11.27)	99.73 (9.09)	2.67 (0.02)*
T2	101.41 (12.57)	97.67 (16.39)	103.45 (10.27)	0.90 (0.38)
T3	99.82 (15.42)	95.33 (17.40)	102.27 (14.51)	0.88 (0.39)
T4	100.29 (18.15)	93.50 (15.40)	104.00 (19.13)	1.15 (0.27)
NTCB				
T1	88.39 (14.79)	86.76 (13.23)	89.30 (16.29)	0.30 (0.77)
T2	95.65 (18.14)	91.84 (13.33)	97.76 (20.78)	0.57 (0.58)
T3	101.19 (18.11)	101.70 (12.89)	100.91 (21.21)	0.08 (0.94)
T4	101.18 (18.72)	97.08 (12.08)	103.46 (21.91)	0.60 (0.56)

For WMI means, (total $n = 17$; adaptive $n = 6$; nonadaptive $n = 11$), for NTCB means (total $n = 14$; adaptive $n = 5$; nonadaptive $n = 9$). T1: preintervention assessment; T2: postintervention assessment; T3: 10–20 weeks postintervention; T4 = final follow-up 6 months after the previous assessment; NTCB: NIH Toolbox Cognition Battery Fluid Cognition Composite; WMI: Wechsler Intelligence Scales Working Memory Index.
*$p < .05$.

T3 or T4 (Table 4). There were no other significant differences between time points. Of note, T2 scores did not significantly differ from T3 or T4 in paired *t*-tests, suggesting scores did not decline after initial gains. The main effect for group and the group × time interaction were nonsignificant. As there were baseline differences between groups on the WMI (Table 5), a follow-up ANCOVA was conducted, with group and time and their interaction included, covarying for T1 WMI. The significant effect of time on postintervention follow-up WMI scores remained, $F(2, 28) = 3.28$, $p = .05$, $\eta^2 = .20$. The main effect for group and the group × time interaction were nonsignificant.

For analyses of the NTCB, the repeated measures ANOVA included Cogmed group as a between-subjects

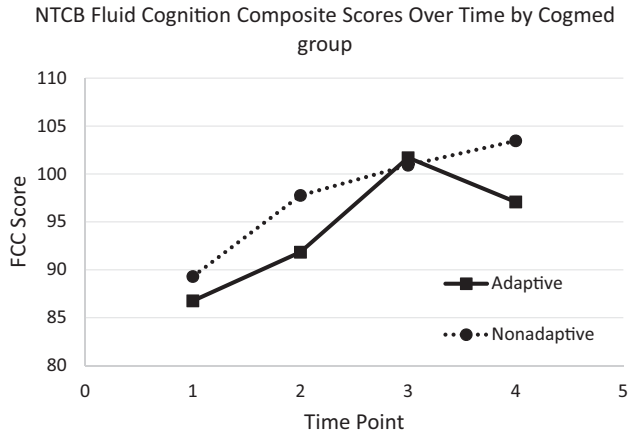

Figure 3. Repeated measures ANOVA of NTCB Fluid Cognition Composite Scores across all time points by Cogmed group.

factor, time as a within-subjects factor, and diagnosis to T1 time as a covariate. There was a significant effect of time on NTCB scores, $F(3, 33) = 8.45$, $p < .001$, $\eta^2 = .43$ (see Figure 3). Post-hoc pairwise comparisons demonstrated that postintervention T2 NTCB scores, $p = .03$, T3 scores, $p < .001$, and T4 scores, $p = .006$, were all significantly higher than pre-intervention T1 scores (Table 4). T3 NTCB scores were significantly higher than T2 scores, $p = .001$. Scores at the other time points were not significantly different. There was no effect of group, and the group × time interaction was nonsignificant.

Parent-reported attention and executive function by group across time

Maximizing sample sizes, we conducted separate repeated measures ANOVAs examining the effects of group and time from T1 to T2, T1 to T3, and T1 to T4 on CBCL Attention Problems and BRIEF Global Executive Composite scores, with time since diagnosis as a covariate. From T1 to T4, there was a significant group effect, $F(1, 18) = 6.16$, $p = .02$, $\eta^2 = .26$, where children in the adaptive Cogmed group had lower BRIEF scores (i.e., fewer problems) ($M = 45.20$) than children in the nonadaptive group ($M = 53.00$). All other models for the BRIEF and CBCL were nonsignificant.

Repeated measures ANOVAs including all time points as the within-subjects factor, Cogmed group as the between-subject factor, and time since surgery as a covariate yielded no significant effects for the BRIEF Global Executive Composite or CBCL Attention Problems Scale; the effects of group and time were nonsignificant, and there was no interaction.

Discussion

Deficits in cognitive function, including working memory and other aspects of executive function, in children diagnosed with and treated for brain tumors are well established (De Ruiter et al., 2013; Robinson et al., 2010, 2013). Interventions to remediate cognitive deficits in pediatric brain tumor survivors have been tested on average 5 years after diagnosis (Carlson-Green et al., 2017; Conklin et al., 2015; Cox et al., 2015; Hardy et al., 2013). Recent evidence suggests that deficits may emerge soon after or even prior to surgery, indicating the potential importance of delivering remedial interventions as early as possible (Fraley et al., 2019; Iuvone et al., 2011; Thigpen et al., 2016). However, to our knowledge, no studies have been conducted to test the feasibility and initial efficacy of cognitive training interventions delivered more quickly postdiagnosis or during adjuvant treatment (i.e., radiation, chemotherapy) for those requiring more intensive treatments. The current study was designed to address this gap. First, we found that Cogmed completion close to diagnosis was low. Second, despite these challenges, participants' cognitive function improved over time.

Overall, enrollment and retainment were difficult for families during this time. Contrary to other studies, participants were invited to enroll immediately postdiagnosis. Participants on average completed three of four assessments over a period of approximately 22 months postdiagnosis. Enrolling families after a new cancer diagnosis is potentially important, yet difficult given the distress and disruption families are experiencing (Rodriguez et al., 2012). Enrollment was made possible by close communication, relationships, and partnering with families and their medical teams, as well as research team flexibility around families' schedules and appointments. However, counter to our first hypothesis, a minority of participants were able to complete the predefined acceptable dose of Cogmed sessions. Most previous studies have shown higher compliance for Cogmed completion in children with brain tumors (Conklin et al., 2015, 2017; Cox et al., 2015; Hardy et al., 2013), while others have found similarly low completion (Hocking et al., 2019). Of note, other studies conducted interventions a minimum of 2 years, and on average 5 years, after completion of all treatment, when completing an at-home online training program may be more feasible and acceptable to families. In addition, children randomized to receive the adaptive Cogmed program were less likely to complete the T2 postintervention follow-up, indicating that these families were potentially overburdened by study procedures (e.g., as the adaptive program becomes increasingly difficult as subjects' performance increases) more so than those randomized to complete the nonadaptive program.

With regard to the second, and primary hypothesis, there was no evidence of greater improvement over time favoring the adaptive as compared to the nonadaptive version of Cogmed. While the adaptive group showed a trend toward larger improvements immediately post-training, this is to be interpreted with caution. However, there were significant main effects for time on WISC-IV WMI and the NTCB Fluid Cognition Composite scores. Specifically, participants in both conditions improved in their performance on the WMI and the NTCB from baseline to immediately postintervention. Although scores on the WMI at the two follow-up points did not differ significantly from baseline T1 scores, the scores immediately postintervention did not differ from follow-ups, suggesting that performance on this

measure did not decline. Further, scores on the NTCB were significantly different from baseline postintervention and at both follow-ups. It is promising that these gains were maintained over time, as other studies have shown improvement only immediately postintervention (Hardy et al., 2013) or have not reported beyond 6 months postintervention (Conklin et al., 2017), whereas our results demonstrate gains up to 12 months postintervention. While the NTCB is designed to control for practice effects (Bauer & Zelazo, 2013, 2014; Gershon et al., 2013), the WISC-IV does not have alternative protocols, and improvement on measures over repeated administrations is possible.

Given that observational studies have shown a steady decline in cognitive function in pediatric brain tumor patients over the course of treatment and into survivorship (Spiegler et al., 2004; Stargatt et al., 2007), the current findings suggest that there may have been a beneficial effect of both the adaptive and nonadaptive versions of Cogmed over time, as performance on the WMI and NTCB not only did not decline, but actually improved. In addition, there was preliminary evidence for fewer parent-reported attention problems for children who completed the adaptive program. These results should be interpreted with caution, as this difference was only seen at the final assessment.

It is important to note that this study, unlike others, had a broader sample including all children with diagnosed brain tumors, not only those with established working memory, attentional, or cognitive deficits. Perhaps children and families in these other studies were more motivated to engage in cognitive remediation as they had documented deficits. Furthermore, treatment type, child age, baseline Full Scale IQ, WMI, BRIEF, and CBCL Attention Problems scores did not predict the number of sessions completed, demonstrating that other factors (e.g., stress, timing) may have contributed to low session completion. While treatment type often confers tumor severity, future research should continue to assess differences in working memory performance and intervention response by tumor characteristics (e.g. size, location).

No significant effects were found on the parent report measures of attention problems, and executive function improvement was seen only at the final follow-up. Of note, scores on both the BRIEF and CBCL fell in the normal range at baseline and throughout the follow-up assessments, suggesting that parents did not report any problems for their children in this study. While this differs from one study finding evidence of problems on these scales for pediatric brain tumor survivors (Hocking et al., 2019), it is similar to other studies reporting average scores on these measures postdiagnosis through 5 years (Knight et al., 2014) and those reporting no change in pre- and postintervention scores (Conklin et al., 2015, 2017).

An important consideration for interpretation of our results and for future research is the timing of this study (i.e., families were approached close to diagnosis). Other research has shown that it is difficult for children with brain tumors and their families to complete assessments close to diagnosis, and our results show that it may be difficult to administer interventions as well (Fraley et al., 2019; Thigpen et al., 2016). Delivery of interventions closer to diagnosis and treatment may be beneficial to mitigate risk for subsequent cognitive decline, but it is also a more stressful and difficult time for families. Utilization of at-home computerized working memory training may be challenging for children while still actively dealing with the stress of their diagnosis, medical appointments, and school assignments. Steps need to be taken to make the Cogmed program more acceptable when families are faced with these multiple challenges if this intervention is delivered closer to diagnosis. Accurate psychoeducation and understanding of cognitive late effects may be valuable in motivating families to pursue and complete interventions (Shultz et al., 2017), and for children who do not have cognitive problems or concerns, perhaps cognitive remediation is not as prioritized as other medical and academic demands. It is possible that remediation interventions are best delivered after the completion of treatment, when stress and appointments have likely decreased, but prior to the onset of late effects. Therefore, interventions may be most optimal in between that of previous interventions (i.e., 5 years postdiagnosis) and the present study (i.e., close to diagnosis). In addition, strong collaboration between medical providers and psychologists will be beneficial in motivating families to complete cognitive remediation programs, and additional supports for families will be helpful to facilitate time and ability to complete them, regardless of when they are delivered.

The current study had several limitations that need to be addressed in future research. First, enrollment of patients and parents in the study near the time of diagnosis and surgery proved difficult and retention of participants in the follow-up assessments was also challenging. This resulted in a small sample size for the primary analyses and concomitantly somewhat low statistical power to detect differences between the Cogmed groups. Previous studies have compared the adaptive version of the Cogmed program to usual care or no treatment, whereas in this study we compared the adaptive version of the program with a nonadaptive version. Therefore, it is expected that effect sizes in this study may be smaller than those found in previous research. Also, we were underpowered to assess additional training factors (e.g., duration) to determine if time spent training varied by Cogmed group. Second, we had limited success in achieving compliance with completion of the optimal dose of the Cogmed program. As a result, we were unable to complete a robust test of the fully prescribed intervention. Studies conducting clinic-based interventions similarly show only slight improvements in child outcomes (Butler et al., 2008; Patel et al., 2009), demonstrating the difficulty in assessing and enacting positive cognitive change in children with brain tumors. Finally, future studies should incorporate parent and child interviews in order to better understand why retention for follow-up assessments and Cogmed completion were difficult for families. This could yield important qualitative information to better tailor interventions to families' needs.

These limitations notwithstanding, the current study suggests several directions for future research. Some studies have shown that baseline cognitive abilities are related to Cogmed completion and cognitive change post-intervention (Hardy et al., 2013; Hocking et al., 2019), and others have shown that increased dose of Cogmed training does not significantly improve outcomes in pediatric brain tumor patients (Carlson-Green et al., 2017); therefore, future research should continue to explore when interventions are best implemented, which dosage is appropriate and feasible, and also for whom these interventions are best targeted. Though one study assessing computerized working memory training combined with parental-problem solving training for parents of children with brain tumors and found similarly low feasibility (Hocking et al., 2019), a combination of interventions to improve outcomes may result in the best outcomes for children (i.e., modifications like reducing environmental distractions, participant attention, teaching self-monitoring, pharmacological intervention, parent/family-based intervention, or physical activity) in addition to working memory training. Furthermore, interventions indirectly targeting cognitive rehabilitation without cognitive strategy training or those targeting other skills (e.g., problem solving) have achieved high adherence (Moscato et al., 2019), shown fewer cognitive problems post-intervention (Richard et al., 2019), and improved quality of life (Wade et al., 2020). Working memory training has received much attention in recent years, but often with limited success and methodological concerns (Redick, 2019), therefore, pursuing other avenues of intervention are also important and may be impactful for families.

In summary, this study was designed to investigate the feasibility and initial effects of a working memory training program completed by children with brain tumors within one year of initial diagnosis. We found significant challenges in the delivery of cognitive remediation during this time, though findings suggest that early intervention can change the trajectory of cognitive decline, highlighting the potential benefits of early intervention, as well as significant challenges. Cognitive remediation and buffering against cognitive late effects in this population is essential and researchers should continue to find innovative ways to make interventions feasible, acceptable, and efficacious for families of children with brain tumors.

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ORCID

Rachel E. Siciliano http://orcid.org/0000-0001-5958-6550
Leandra Desjardins http://orcid.org/0000-0002-0455-169X
Ellen H. Steele http://orcid.org/0000-0002-0106-8803
Sohee Park http://orcid.org/0000-0003-3797-4776

Data availability statement

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

References

Achenbach, T. M., & Rescorla, L. A. (2001). *Manual for the ASEBA school-age forms and profiles: An integrated system of multi-informant assessment*. Aseba.

Araujo, G. C., Antonini, T. N., Anderson, V., Vannatta, K. A., Salley, C. G., Bigler, E. D., Taylor, H. G., Gerhardt, C., Rubin, K., Dennis, M., Lo, W., MacKay, M. T., Gordon, A., Hajek Koterba, C., Gomes, A., Greenham, M., & Owen Yeates, K. (2017). Profiles of executive function across children with distinct brain disorders: Traumatic brain injury, stroke, and brain tumor. *Journal of the International Neuropsychological Society*, *23*(7), 529–538. https://doi.org/10.1017/S1355617717000364

Bauer, P. J., & Zelazo, P. D. (2013). IX. NIH Toolbox Cognition Battery (CB): summary, conclusions, and implications for cognitive development. *Monographs of the Society for Research in Child Development*, *78*(4), 133–146. https://doi.org/10.1111/mono.12039

Bauer, P. J., & Zelazo, P. D. (2014). The national institutes of health toolbox for the assessment of neurological and behavioral function: A tool for developmental science. *Child Development Perspectives*, *8*(3), 119–124. https://doi.org/10.1111/cdep.12080

Butler, R. W., Copeland, D. R., Fairclough, D. L., Mulhern, R. K., Katz, E. R., Kazak, A. E., Noll, R. B., Patel, S. K., & Sahler, O. J. Z. (2008). A multicenter, randomized clinical trial of a cognitive remediation program for childhood survivors of a pediatric malignancy. *Journal of Consulting and Clinical Psychology*, *76*(3), 367–378. https://doi.org/10.1037/0022-006X.76.3.367.A

Carlson-Green, B., Puig, J., & Bendel, A. (2017). Feasibility and efficacy of an extended trial of homebased working memory training for pediatric brain tumor survivors: A pilot study. *Neuro-Oncology Practice*, *4*(2), 111–120. https://doi.org/10.1093/nop/npw015

Conklin, H. M., Ashford, J. M., Clark, K. N., Martin-Elbahesh, K., Hardy, K. K., Merchant, T. E., Ogg, R. J., Jeha, S., Huang, L., & Zhang, H. (2017). Long-term efficacy of computerized cognitive training among survivors of childhood cancer: A single-blind randomized controlled trial. *Journal of Pediatric Psychology*, *42*(2), 220–231.https://doi.org/10.1093/jpepsy/jsw057

Conklin, H. M., Ashford, J. M., Howarth, R. A., Merchant, T. E., Ogg, R. J., Santana, V. M., Reddick, W. E., Wu, S., & Xiong, X. (2012). Working memory performance among childhood brain tumor survivors. *Journal of the International Neuropsychological Society*, *18*(6), 996–1005. https://doi.org/10.1017/S1355617712000793

Conklin, H. M., Helton, S., Ashford, J., Mulhern, R. K., Reddick, W. E., Brown, R., Bonner, M., Jasper, B. W., Wu, S., Xiong, X., & Khan, R. B. (2010). Predicting methylphenidate response in long-term survivors of childhood cancer: A randomized, double-blind, placebo-controlled, crossover trial. *Journal of Pediatric Psychology*, *35*(2), 144–155. https://doi.org/10.1093/jpepsy/jsp044

Conklin, H. M., Khan, R. B., Reddick, W. E., Helton, S., Brown, R., Howard, S. C., Bonner, M., Christensen, R., Wu, S., Xiong, X., & Mulhern, R. K. (2007). Acute neurocognitive response to methylphenidate among survivors of childhood cancer: A randomized, double-blind, cross-over trial. *Journal of Pediatric Psychology*, *32*(9), 1127–1139. https://doi.org/10.1093/jpepsy/jsm045

Conklin, H. M., Lawford, J., Jasper, B. W., Morris, E. B., Howard, S. C., Ogg, S. W., Wu, S., Xiong, X., & Khan, R. B. (2009). Side effects of methylphenidate in childhood cancer survivors: A randomized placebo-controlled trial. *Pediatrics*, *124*(1), 226–233. https://doi.org/10.1542/peds.2008-1855

Conklin, H. M., Ogg, R. J., Ashford, J. M., Scoggins, M. A., Zou, P., Clark, K. N., Martin-Elbahesh, K., Hardy, K. K., Merchant, T. E., Jeha, S., Huang, L., & Zhang, H. (2015). Computerized cognitive training for amelioration of cognitive late effects among childhood cancer survivors: A randomized controlled trial. *Journal of Clinical Oncology*, *33*(33), 3894–3902. https://doi.org/10.1200/JCO.2015.61.6672

Coomans, M. B., van der Linden, S. D., Gehring, K., & Taphoorn, M. J. B. (2019). Treatment of cognitive deficits in brain tumour patients: current status and future directions. *Current Opinion in Oncology*, *31*(6), 540–547. https://doi.org/10.1097/CCO.0000000000000581

Cox, L. E., Ashford, J. M., Clark, K. N., Martin-Elbahesh, K., Hardy, K. K., Merchant, T. E., Ogg, R. J., Jeha, S., Willard, V. W., Huang, L., Zhang, H., & Conklin, H. M. (2015). Feasibility and acceptability of a remotely administered computerized intervention to address cognitive late effects among childhood cancer survivors. *Neuro-oncology Practice*, *2*(2), 78–87. https://doi.org/10.1093/nop/npu036

De Ruiter, M. A., Van Mourik, R., Schouten-Van Meeteren, A. Y. N., Grootenhuis, M. A., & Oosterlaan, J. (2013). Neurocognitive consequences of a paediatric brain tumour and its treatment: A meta-analysis. *Developmental Medicine and Child Neurology*, *55*(5), 408–417. https://doi.org/10.1111/dmcn.12020

Duda, T. A., Ris, M. D., Yeates, K. O., Mahone, E. M., Haut, J. S., & Raghubar, K. P. (2020). Reliable change in pediatric brain tumor: A preliminary investigation. *Child Neuropsychology*, *26*(1), 15–26. https://doi.org/10.1080/09297049.2019.1620715

Fraley, C. E., Thigpen, J., Pearson, M. M., Kuttesch Jr, J. F., Desjardins, L., Hoskinson, K. R., Alvarado-Gonzalez, A., Esbenshade, A. J., Pastakia, D., Friedman, D. L., Wellons, J. C., McNally, C. M., Siciliano, R. E., & Compas, B. E. (2019). Predictors of cognitive function in pediatric brain tumor patients: Pre-surgery through 24-month follow-up. *Applied Neuropsychology: Child*. https://doi.org/10.1080/21622965.2019.1706179

Gershon, R. C., Wagster, M. V., Hendrie, H. C., Fox, N. A., Cook, K. F., & Nowinski, C. J. (2013). NIH toolbox for assessment of neurological and behavioral function. *Neurology*, *80*(Issue 11, Supplement 3), S2–S7. https://doi.org/10.1212/WNL.0b013e3182872e5f

Gioia, G. A., Isquith, P. K., Guy, S. C., & Kenworthy, L. (2000). Test review behavior rating inventory of executive function. *Child Neuropsychology*, *6*(3), 235–238.

Gioia, G. A., Isquith, P. K., & Kenealy, L. E. (2008). Assessment of behavioral aspects of executive function. In V. Anderson, R. Jacobs, & P. J. Anderson (Eds.), *Neuropsychology, neurology, and cognition. Executive functions and the frontal lobes: A lifespan perspective* (pp. 179–202). Taylor & Francis.

Gray, S. A., Chaban, P., Martinussen, R., Goldberg, R., Gotlieb, H., Kronitz, R., Hockenberry, M., & Tannock, R. (2012). Effects of a computerized working memory training program on working memory, attention, and academics in adolescents with severe LD and comorbid ADHD: A randomized controlled trial. *Journal of Child Psychology and Psychiatry, and Allied Disciplines*, *53*(12), 1277–1284. https://doi.org/10.1111/j.1469-7610.2012.02592.x

Hardy, K. K., Willard, V. W., Allen, T. M., & Bonner, M. J. (2013). Working memory training in survivors of pediatric cancer: A randomized pilot study. *Psycho-oncology*, *22*(8), 1856–1865. https://doi.org/10.1002/pon.3222

Hocking, M. C., Paltin, I., Quast, L. F., & Barakat, L. P. (2019). Acceptability and feasibility in a pilot randomized clinical trial of computerized working memory training and parental problem-solving training with pediatric brain tumor survivors. *Journal of Pediatric Psychology*, *44*(6), 669–678. https://doi.org/10.1093/jpepsy/jsz015

Iuvone, L., Peruzzi, L., Colosimo, C., Tamburrini, G., Caldarelli, M., Di Rocco, C., Battaglia, D., Guzzetta, F., Misciagna, S., Di Giannatale, A., Ruggiero, A., & Riccardi, R. (2011). Pretreatment neuropsychological deficits in children with brain tumors. *Neuro-oncology*, *13*(5), 517–524. https://doi.org/10.1093/neuonc/nor013

Kirschen, M. P., Davis-Ratner, M. S., Milner, M. W., Chen, S. H. A., Schraedley-Desmond, P., Fisher, P. G., & Desmond, J. E. (2008). Verbal memory impairments in children after cerebellar tumor resection. *Behavioural Neurology*, *20*(1–2), 39–53. https://doi.org/10.3233/BEN-2008-0216

Knight, S. J., Conklin, H. M., Palmer, S. L., Schreiber, J. E., Armstrong, C. L., Wallace, D., Bonner, M., Swain, M. A., Evankovich, K. D., Mabbott, D. J., Boyle, R., Huang, Q., Zhang, H., Anderson, V. A., & Gajjar, A. (2014). Working memory abilities among children treated for medulloblastoma: Parent report and child performance. *Journal of Pediatric Psychology*, *39*(5), 501–511. https://doi.org/10.1093/jpepsy/jsu009

Law, N., Bouffet, E., Laughlin, S., Laperriere, N., Brière, M. E., Strother, D., McConnell, D., Hukin, J., Fryer, C., Rockel, C., Dickson, J., & Mabbott, D. (2011). Cerebello-thalamo-cerebral connections in pediatric brain tumor patients: Impact on working memory. *NeuroImage*, *56*(4), 2238–2248. https://doi.org/10.1016/j.neuroimage.2011.03.065

Mabbott, D. J., Penkman, L., Witol, A., Strother, D., & Bouffet, E. (2008). Core neurocognitive functions in children treated for posterior fossa tumors. *Neuropsychology*, *22*(2), 159–168. https://doi.org/10.1037/0894-4105.22.2.159

Moscato, E. L., Miley, A. E., LeBlond, E. I., King, J. A., Raj, S. P., Narad, M. E., Platt, A., Thompson, A. N., Baum, K. T., Salloum, R., & Wade, S. L. (2019). Feasibility and acceptability of an online problem-solving therapy intervention for adolescent and young adult brain tumor survivors. *Clinical Practice in Pediatric Psychology*, *7*(1), 68–78. https://doi.org/10.1037/cpp0000265

Ostrom, Q. T., Gittleman, H., Xu, J., Kromer, C., Wolinsky, Y., Kruchko, C., & Barnholtz-Sloan, J. S. (2016). CBTRUS statistical report: Primary brain and other central nervous system tumors diagnosed in the United States in 2009–2013. *Neuro-oncology*, *18*(suppl_5), v1–v75. https://doi.org/10.1093/neuonc/now207

Palmer, S. L., Armstrong, C., Onar-Thomas, A., Wu, S., Wallace, D., Bonner, M. J., Schreiber, J., Swain, M., Chapieski, L., Mabbott, D., Knight, S., Boyle, R., & Gajjar, A. (2013). Processing speed, attention, and working memory after treatment for medulloblastoma: An international, prospective, and longitudinal study. *Journal of Clinical Oncology*, *31*(28), 3494–3500. https://doi.org/10.1200/JCO.2012.47.4775

Patel, S. K., Katz, E. R., Richardson, R., Rimmer, M., & Kilian, S. (2009). Cognitive and problem solving training in children with cancer: A pilot project. *Journal of Pediatric Hematology/Oncology*, *31*(9), 670–677. https://doi.org/10.1097/MPH.0b013e3181b25a1d

Redick, T. S. (2019). The hype cycle of working memory training. *Current Directions in Psychological Science*, *28*(5), 423–429. https://doi.org/10.1177/0963721419848668

Richard, N. M., Bernstein, L. J., Mason, W. P., Laperriere, N., Maurice, C., Millar, B. A., Shultz, D. B., Berlin, A., & Edelstein, K. (2019). Cognitive rehabilitation for executive dysfunction in brain tumor patients: A pilot randomized controlled trial. *Journal of Neuro-Oncology*, *142*(3), 565–575. https://doi.org/10.1007/s11060-019-03130-1

Robinson, K. E., Fraley, C. E., Pearson, M. M., Kuttesch, J. F., & Compas, B. E. (2013). Neurocognitive late effects of pediatric brain tumors of the posterior fossa: A quantitative review. *Journal of the International Neuropsychological Society*, *19*(1), 44–53. https://doi.org/10.1017/S1355617712000987

Robinson, K. E., Kuttesch, J. F., Champion, J. E., Andreotti, C. F., Hipp, D. W., Bettis, A. H., Barnwell, A. S., & Compas, B. E. (2010). A quantitative meta-analysis of neurocognitive sequelae in survivors of pediatric brain tumors. *Pediatric Blood and Cancer*, *55*(3), 525–531. https://doi.org/10.1002/pbc.22568

Rodriguez, E. M., Dunn, M. J., Zuckerman, T., Vannatta, K., Gerhardt, C. A., & Compas, B. E. (2012). Cancer-related sources of stress for children with cancer and their parents. *Journal of Pediatric Psychology*, *37*(2), 185–197. https://doi.org/10.1093/jpepsy/jsr054

Shultz, E. L., Lehmann, V., Rausch, J. R., Keim, M. C., Winning, A. M., Olshefski, R. S., Vannatta, K. A., Compas, B. E., & Gerhardt, C. A. (2017). Family estimates of risk for neurocognitive late effects

following pediatric cancer: From diagnosis through the first three years of survivorship. *Pediatric Blood and Cancer*, *64*(9), 1–7. https://doi.org/10.1002/pbc.26462

Siegel, D. A., Richardson, L. C., Henley, S. J., Wilson, R. J., Dowling, N. F., Weir, H. K., Tai, E. W., & Buchanan Lunsford, N. (2020). Pediatric cancer mortality and survival in the United States, 2001–2016. *Cancer*, *126*(19), 4379–4389. https://doi.org/10.1002/cncr.33080

Spiegler, B. J., Bouffet, E., Greenberg, M. L., Rutka, J. T., & Mabbott, D. J. (2004). Change in neurocognitive functioning after treatment with cranial radiation in childhood. *Journal of Clinical Oncology*, *22*(4), 706–713. https://doi.org/10.1200/JCO.2004.05.186

Stargatt, R., Rosenfeld, J. V., Maixner, W., & Ashley, D. (2007). Multiple factors contribute to neuropsychological outcome in children with posterior fossa tumors. *Developmental Neuropsychology*, *32*(2), 729–748. https://doi.org/10.1080/87565640701376151

Thigpen, J. C., Pearson, M., Robinson, K. E., Andreotti, C., Dunbar, J. P., Watson, K. H., Dejardins, L., Holmes, L., Byram, R., Fraley, C., & Compas, B. E. (2016). Presurgical assessment of cognitive function in pediatric brain tumor patients: Feasibility and initial findings. *Neuro-oncology Practice*, *3*(4), 261–267. https://doi.org/10.1093/nop/npv066

Tonning Olsson, I., Perrin, S., Lundgren, J., Hjorth, L., & Johanson, A. (2014). Long-term cognitive sequelae after pediatric brain tumor related to medical risk factors, age, and sex. *Pediatric Neurology*, *51*(4), 515–521. https://doi.org/10.1016/j.pediatrneurol.2014.06.011

Wade, S. L., Narad, M. E., Moscato, E. L., LeBlond, E. I., King, J. A., Raj, S. P., Platt, A., Thompson, A. N., Baum, K. T., & Salloum, R. (2020). A survivor's journey: Preliminary efficacy of an online problem-solving therapy for survivors of pediatric brain tumor. *Pediatric Blood and Cancer*, *67*(2), 1–8. https://doi.org/10.1002/pbc.28043

Wechsler, D. (2003). *WISC-IV: Wechsler intelligence scale for children* (4th ed.). The Psychological Corporation.

Wechsler, D. (2011). *WASI-II: Wechsler abbreviated scale of intelligence* (2nd ed.). NCS Pearson.