2018

Cognitive Remediation Of Working Memory Deficits In Children With Chronic Health Conditions: Tailoring Cogmed Training To Address Barriers To Adherence

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COGNITIVE REMEDIATION OF WORKING MEMORY DEFICITS IN CHILDREN WITH CHRONIC HEALTH CONDITIONS: TAILORING COGMED TRAINING TO ADDRESS BARRIERS TO ADHERENCE

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Submitted in Partial Fulfillment of the Requirements

For the Degree of Doctor of Philosophy in

Clinical-Community Psychology

College of Arts and Sciences

University of South Carolina

2018

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ACKNOWLEDGMENTS

I would like to acknowledge all of the families that participated in my research study as well as the wonderful staff, physicians and nurses at the Center for Children with Cancer and Blood Disorders at Palmetto Health. I would also like to thank my mentor, Dr. Jeffrey Schatz, who has supported me in the process and allowed me to pursue my interest in cognitive remediation. I would also like to thank my husband, Stephen, my parents, Kathy and Kevin, and my sister Meghan for all of your support throughout the years. I couldn't have done this without you!

ABSTRACT

Objective: Children with sickle cell disease (SCD) and cancer are at risk for working memory impairment due to the disease and treatment. However, inconsistency in adherence to cognitive training programs conducted with this population suggests that adaptations are necessary in order to improve the effectiveness of this intervention. In addition, it is unclear whether gains in working memory translate to improvement in classroom functioning.

Methods: Children engaged in cognitive training exclusively over the summer in order to improve adherence to Cogmed Working Memory Training. A total of 17 children ages 7-17 with a diagnosis of SCD (n = 14) and cancer (n = 3) were enrolled in the study. Of the 17 children, 5 children completed the program (at least 80% of sessions), 5 children completed between 8 and 15 sessions, and 7 children did not complete any sessions. I conducted further analyses to measure changes in working memory performance from time 1 to time 2 on the WISC-V as well as generalizability to a measure of functional attention performance. I also collected parent feasibility ratings.

Results: Parents generally endorsed that training during the summer was convenient (77.8%) and would recommend Cogmed to others. However, adherence rates did not exceed 80% as hypothesized. Follow-up analyses indicated a non-significant improvement in group means on the WISC-V Working Memory Composite Score or

individual working memory subtests for all groups. However, changes in group means showed a large effect size for completers, $t(4) = -1.66$, $p = .17$, d = .87 and a medium effect for partial completers, $t(4) = -.62$, $p = .57$, d = .37. Conversely, group means for the Working Memory Composite showed only a small effect for non-completers, $t(3) = -.34$, $p = .76$, d = .10. Similar effect sizes were found for the Digit Span and Letter-Number Sequencing subtests but not the Picture Span subtest. The hypothesis that gains in working memory would generalize to measures of functional attention and working memory was not supported.

Conclusions: Overall, this study demonstrates that training over the summer does not significantly increase adherence to the program but may serve as a feasible option for many families with a child with a chronic illness. Although the sample size was too small to detect a statistically significant increase in working memory, effect sizes were of medium size in partial completers and large in completers, suggesting comparable effects as studies with larger samples that have demonstrated efficacy. Differences in baseline attention skills for completers versus non-completers suggest that the TEA-Ch, a measure of functional attention, may be an important tool for selecting children most likely to complete the full program. Further research with larger samples sizes is needed in order to confirm study results and test alternative methods for improving adherence in this population.

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INTRODUCTION

Cognitive training is an innovative method for remediating problems in cognition in children. Research in this area demonstrates that cognitive training methods are effective for healthy children in improving general intelligence (Bracy, et al., 1999), working memory (Dunning, Holmes, & Gathercole, 2013; Nutley, et al., 2011; Goldin, et al., 2013; Holmes, Gathercole, & Dunning, 2009; Kroesbergen, Van't Noordende, & Kolkman, 2014; Loosli et al., 2012; Thorell et al., 2009), attention (Goldin et al., 2014; Rueda, Checa, & Combita, 2012) and processing speed (Mackey et al., 2011). Cognitive training is also effective in children with cognitive impairment from a health condition (Hardy et al., 2013; Hovik et al., Slomine & Locascio, 2009). However, the majority of literature on cognitive training in this population has been conducted with children diagnosed with ADHD or children that have sustained a traumatic brain injury. Less research has been conducted in children with other chronic health conditions such as sickle cell disease (SCD) or cancer. Due to the heterogeneity of the source of cognitive impairment from SCD or cancer as well as medical complications from the disease, these children have unique considerations that may impact the effectiveness of cognitive training programs. Individual differences such as etiology of cognitive impairment may not only impact effectiveness of cognitive training (Shah, Buschkuehl, Jaeggi, & Jonides, 2012) but also whether or not cognitive training transfers to untrained cognitive skills

(Jaeggi, Buschkuehl, Shah, & Jonides, 2013) and classroom working memory functioning. In addition, inconsistency in adherence to cognitive training programs conducted with children with SCD or cancer suggests that adaptations are necessary in order to improve the effectiveness of this intervention.

What is Cognitive Training?

Cognitive training is an innovative therapeutic approach that has been successful in improving cognitive deficits in a variety of illness populations. Through repeated instructional practice, cognitive training methods reinforce, strengthen, or reestablish previously learned patterns of behavior and establish new patterns of cognition through compensatory cognitive mechanisms (Butler, 1998; Cicerone et al., 2000) in the areas of language, attention, concentration, spatial perception, memory, calculation, and working memory (Cappa, 2005; Cicerone et al., 2000; Klingberg, Forssberg, & Westerberg, 2002). Cognitive training is based on Luria's theory of brain function, which suggests that cognitive skills rely on collaboration of different brain areas, which merge into functional brain systems. These complex networks have the capacity to compensate for damage and correct dysfunction through reorganization, particularly in the growing brain (Berlucchi, 2011; Mikadze, 2014). Due to this plasticity, the brain is not only able to compensate for the damage through circumventing the disability, but is also able to substitute the cognitive skill with a new method of performing a task through training over and above what the patient would have been able to achieve without intervention (Berlucchi, 2011).

Cognitive training is directed toward many areas of cognition, including attention, concentration, perception, memory, comprehension, communication, reasoning, problem solving, judgment, imitation, planning, self-monitoring, and awareness (Cicerone et al., 2000). A range of methods have been used to train cognitive skills. For example, the Amsterdam Memory and Attention for Children (AMAT-C) program uses daily practice and games as well as exercises in attention and memory in order to remediate deficits. Additional techniques are applied that teach children strategies that they can use in their daily lives in order to accomplish school tasks (Van't Hooft et al., 2005). In the Pay Attention program, children practice attention and executive functions using cognitive operations and subsequently receive corrective feedback for errors in order to improve accuracy and speed in the future (Chenault, Thomson, Abbott, & Berninger, 2006). Perhaps the most popular method that has shown to be effective in recent years is cognitive training through computerized methods.

Computer cognitive retraining methods are an interactive and interesting approach for children to engage in practicing cognitive skills and are effective at improving working memory in patients with stroke (Westerberg et al., 2007) and children with ADHD (Klingberg, Forssberg, & Westerberg, 2002b). Training through a computerized program is convenient, effective, and is lower cost than other methods (Matthews, Harley, & Malec, 1991). Skills learned through computerized cognitive training show transfer to certain aspects of executive function and measures of school performance in typically developing children (Goldin et al., 2014). CogMed is an example of an adaptive computerized working memory program that trains children in verbal and visuospatial working memory and has been effective in improving working memory in children with a range of diagnoses (Beck et al., 2010; Chacko et al., 2014; Hardy, Willard, Allen, & Bonner, 2013). Other examples of computerized working programs are

Jungle Memory (http://www.junglememory.com) and Cognifit (http://www.cognifit.com) (Melby-Lervag, 2013).

Imaging studies of cognitive training show that in addition to improvements on measures of cognitive functioning, cognitive training is associated with changes in cortical activity in the neural systems underlying specific cognitive functions (Jolles et al., 2013; Olesen, Westerberg, & Klingberg, 2004). For example, Olesen and colleagues found increased functional connectivity in the middle frontal gyrus and the superior and inferior parietal cortices after working memory training (2004). The amount of working memory training completed is associated with increased structural connectivity in white matter regions adjacent to the intraparietal sulcus and the anterior part of the body of the corpus callosum, regions critical in working memory (Takeuchi et al., 2010).

Does Cognitive Training Work for Healthy Children?

Cognitive training has been used to remediate a variety of problems in healthy children including working memory (Alloway, Bibile, & Lau, 2013; Dunning, Holmes, & Gathercole, 2013; Goldin et al., 2013; Nutley, et al., 2011**)**, intelligence (Bracy, et al., 1999**)**, attention (Goldin, et al., 2014; Rueda, Checa, & Combita, 2012), mathematical ability (Barkl, Porter, & Ginns, 2012; Holmes, Gathercole, & Dunning, 2009; Kroesbergen, Van't Noordende, & Kolkman, 2014), fluid reasoning and processing speed (Mackey et al., 2011). Studies conducted on working memory training in healthy children have found that working memory training leads to improvement on non-trained working memory tasks (Dunning, Holmes, & Gathercole, 2013; Klingberg, Forssberg, & Westerberg, 2002b) as well improvements in verbal (Alloway, Bibile & Lau, 2013; Loosli et al., 2012) and mathematics abilities (Goldin et al, 2014).

Effects from cognitive training seem to be maintained three months (Barkl, Porter, & Ginns, 2012), eight months (Alloway, Bibile & Lau, 2013), and one year after training (Dunning, Holmes, & Gathercole, 2013). In studies of healthy children, training has proven to be effective in children as young as four years (Nutley et al., 2011; Thorell et al., 2009) up to adolescence (Bracy et al., 1999; Navarro et al., 2003). Most of the recent research in cognitive training in healthy children has used computerized training methods (Alloway, Bibile, & Lau, 2013; Bracy et al., 1999; Holmes, Gathercole, & Dunning, 2009; Loosli et al., 2012; Nutley et al., 2011). Among studies that focus on working memory training, research has shown that this method has a significant impact on both visual spatial and verbal working memory (Holmes, Gathercole, & Dunning, 2009; Thorell et al., 2009).

Cognitive Training in Children with Cancer

Cognitive training has been used with children with cancer to effectively remediate problems in the areas of attention and concentration (Butler, 2002; Butler et al., 2008; Hardy, Willard, & Bonner; Kesler, Lacayo, & Jo, 2011; Patel, Katz, Richardson, Rimmer, & Kilian, 2009; Van't Hooft & Norberg, 2010), working memory (Conklin et al., 2015; Hardy, Willard, Allen, & Bonner, 2013; Hardy, Willard, & Bonner, 2011; Kesler, Lacayo, & Jo, 2011; Van't Hooft & Norberg, 2010), and academic achievement (Butler et al., 2008; Patel et al., 2009). Furthermore, studies have shown evidence that cognitive training leads to changes in brain activity among childhood cancer survivors (Conklin et al., 2015; Zou et al., 2012). Sample sizes have varied between small pilot studies of three children (Van't Hooft & Norberg, 2010) and larger multi-site randomized trials (Butler et al., 2008). Cognitive training conducted in children with cancer has been applied to children as young as 6 years up to 22 years (Butler & Copeland, 2002). Across these interventions, there is great variability in the time that it takes to complete a cognitive training program with some programs lasting a total of 5 weeks (Hardy et al., 2013; Hardy, Willard, & Bonner, 2011) and others lasting up to six months (Butler et al., 2008). In addition, adherence across studies varies between 28% (Patel et al., 2009) and 100% (Hardy, Willard, & Bonner, 2011; Van't Hooft, 2010), with the best adherence cited in studies with small samples sizes.

Several methods have been used in order to implement cognitive training with children with cancer. One promising avenue of research combines cognitive training with additional strategies including cognitive behavioral therapy (CBT) and metacognitive strategies to reinforce training (Butler & Copeland, 2002; Butler et al., 2008; Patel, et al., 2009). This method has been shown to aid childhood cancer survivors in improving working memory, academic achievement and parent-reported attention as well as increase use of metacognitive strategies (Butler et al., 2008). The Swedish Memory and Attention Retraining (SMART) program uses a combination of daily practice and games, exercises in specific attention and memory techniques, and therapeutic behavior techniques that focus on relaxation and the accomplishment of school tasks. In a small pilot study (n =3), the program improved sustained and selective attention, visual spatial memory, and verbal memory. However, executive functioning problems slightly increased after training according to teacher ratings. Furthermore, parents reported that daily practice sessions interfered with the child's schedule (Van't Hooft & Norberg, 2010).

Other studies have incorporated techniques to compensate for individual differences and environmental factors on the success of cognitive training. In one intervention study conducted with children with cancer, the program was tailored toward the child's own strengths and weaknesses. In addition, the child's therapist collaborated with the child's parent and the child's teacher in order to optimize success in the training. This program led to significant improvement in comparison to controls in the areas of attention and concentration including improvement on measures of digit span, sentence memory, and a continuous performance test (Butler & Copeland, 2002). Cognitive training using exclusively strategy training has also been tested in children with cancer. In a study of pediatric cancer survivors, children learned problem-solving skills, behavioral study skills and metacognitive strategies, self-monitoring, self-motivation, and self-reinforcement. The children also learned information processing strategies, techniques such as chunking, reorganizing information into semantic categories, associating new information to material that has been learned previously, mnemonic devices, visual imagery, and using repetition through multimodal input. However, these strategies did not result in a statistically significant change in functioning (Patel et al., 2009).

In contrast to in-person cognitive training methods, computerized training allows more flexibility and less staff resources. For example, the child and parent can decide what time is best to complete the training, depending on individual schedules and medical needs. In addition, this method does not require staff resources to administer each training session. To date, computerized training has been successful implemented at home (Conklin et al., 2015; Cox et al., 2015; Hardy, Willard, Allen & Bonner, 2013;

Hardy, Willard, & Bonner, 2011; Kesler, Lacayo, & Jo, 2011), but has not been tested in a school or a clinic setting. Programs that have been used in order to train cognitive abilities include Captain's log (Hardy, Willard, & Bonner, 2011) and Lumos Labs cognitive exercise program (Kesler, Lacayo, & Jo, 2011). In a study of nine children with CNS affecting cancer using Captian's Log, children improved on measures of attention including parent report and Digit Span forward, but did not improve on some measures of working memory including Digit Span Backward and Letter-Number Sequencing. The authors reported that there was significant variation in the amount of time spent on the intervention, ranging from 9 to 53 sessions and from 3.7 to 20.8 training hours, suggesting that there were possible difficulties with finding time to conduct the training during the day (Hardy, Willard, & Bonner, 2011). Children with a history of brain tumors and ALL (Acute Lymphoblastic Leukemia) trained with Lumos Labs exercise program improved processing speed, executive functioning, verbal memory, and visual memory. Working memory did not improve from time one to time two. Although the program was expected to last for eight weeks, most children required an average of 14 weeks to complete training (Kesler, Lacayo, & Jo, 2011).

Perhaps the most effective and widely used at-home method for cognitive training in children with a history of brain tumor or ALL is Cogmed Working Memory Training (Conklin et al., 2015; Cox et al., 2015; Hardy, Willard, Allen & Bonner, 2013). The evidence suggests that Cogmed improves working memory and processing speed and reduces parent-reported symptoms of inattention, executive function, and learning problems (Conklin et al., 2015; Hardy, Willard, Allen & Bonner, 2013). In addition, Cogmed is associated with a reduction in fMRI prefrontal and parietal activation, suggesting that training increases neural network efficiency in brain regions associated with working memory (Conklin et al., 2015). Overall, parents and children that participate in computerized cognitive training programs report satisfaction with this method of training and report few issues with technological problems (Cox et al., 2015; Hardy, Willard, Allen & Bonner, 2013). However, more research is needed to determine the generalizability of this method to other cognitive skills as well as the long-term impact of training on working memory (Conklin et al., 2015; Hardy, Willard, Allen & Bonner, 2013).

Cognitive Training in Children with Sickle Cell Disease

To date, only three studies have been published on cognitive training with children with SCD, despite the increased risk for stroke and other sources of neurocognitive deficit that warrant inclusion in cognitive training studies. Two of the studies to date used strategy training methods, including silent rehearsal to facilitate short-term memory and semantic clustering to facilitate long-term memory (King et al., 2007; Yerys et al., 2003). For example, in a study following six children ages 11-15 with SCD with a history of infarct, two out of three children who received strategy training improved on measures of short-term memory and all three children improved on measures of long-term memory (Yerys et al., 2003). In another study of strategy training conducted with 11 children with SCD and a history cerebral infarct, children in the intervention group improved on measures of working memory compared to the control group. Both the control and intervention groups improved on academic achievement (King et al., 2007). In addition, both of these studies conducted cognitive training using strategy training rather than adaptive cognitive training, which has generally been found to be more effective in remediating problems.

The most robust study of cognitive training examined the feasibility of using Cogmed working memory training in 12 children and adolescents with SCD ages 7-16 years. The data from this study suggest that working memory training is effective in improving performance on trained and untrained working memory tasks including tests measuring either verbal or spatial working memory; researchers in this study, however, also commented on issues with adherence, citing an overall adherence rate of approximately 50% (Hardy et al., 2016). Although this study demonstrates that computerized cognitive training has been effective in remediating problems in working memory in children with SCD, more research with larger sample sizes is needed. In addition, future studies need to address issues of adherence in this population.

Importance of Working Memory

Working memory involves the short-term maintenance and manipulation of information, which is important for tasks such as encoding information into long-term memory (learning), auditory comprehension, and reasoning (Baddeley, 2003). Working memory is also considered to be a critical function for most forms of higher-level cognition (McCabe, 2010). Furthermore, working memory is associated with academic ability (Alloway, 2004) and general intelligence (Conway, Kane, & Engle, 2003; Waiter et al., 2009) in children. In fact, it is difficult to separate working memory from intelligence due to the impact of working memory on cognitive skills such as reading and mathematics (Bull & Scerif, 2001; Gathercole et al., 2006) and evidence of similar underlying structures in working memory and intelligence (Kuwajima & Sawaguchi, 2010).

As children age, working memory capacity increases. Imaging studies show that older children show increased brain activity on a functional MRI (fMRI) in the superior frontal and intraparietal cortex than younger children while performing working memory tasks. These frontal and parietal regions are involved in the control of attention and spatial working memory (Klingberg, Forssberg, & Westerberg, 2002). However, some children demonstrate impairment in working memory. Typically four to five students in a classroom of thirty will demonstrate significantly impaired working memory (Gathercole & Alloway, 2008). Children with special education needs, however, are sixteen times more likely to exhibit problems in working memory, with particular difficulty with tasks involving the central executive (Alloway, Gathercole, Adams, & Willis, 2005).

Adults and children with SCD show impairment on tasks of working memory at a higher rate than typically developing children (White, Salorio, Schatz & DeBaun, 2000; Vichinsky et al., 2010). Working memory is related to the ability to control attention, particularly under conditions that involve distraction or interference (Engle & Kane, 2004). Due to the evidence that children with SCD demonstrate problems with selective attention, children with SCD may also exhibit greater deficits in working memory (Craft et al., 1994; Schatz et al., 2001; Schatz, Craft, & Koby, 2000). Children with SCD who have experienced a stroke are at greater risk for deficits in working memory (Brandling-Bennett, 2003; White, et al., 2000), with specific damage to key prefrontal regions (e.g., dorsolateral prefrontal cortex) associated with problems related to manipulating information in working memory (Brandling-Bennett, 2003).

Deficits in working memory also occur in children receiving treatment for ALL (Ashford et al., 2010; Carey et al., 2007; de Oliveira-Gomes, Leite, Garcia, Maranhao, & Hazin, 2012) and brain tumors (Conklin et al., 2012; Dennis, Hetherington, & Spiegler, 1998). For children with ALL, these deficits may be evident as early as the first year of treatment, with severity of deficits dependent on the dose of methotrexate and the rate of infusion (Carey et al., 2007). Children receiving cranial radiation treatment for brain tumors seem to exhibit poorer working memory than children with brain tumors that did not receive radiation treatment (Dennis, Hetherington, & Spiegler, 1998). Working memory may be the best indicator of treatment-related changes in children with cancer due to evidence that working memory measures seem to be more sensitive than global intelligence measures (Ashford et al., 2010).

Working memory is an important target for intervention in children with SCD and cancer due to the significance of deficits in working memory on overall cognitive functioning and the prevalence of problems in working memory in this population. Although literature in this area has not been extensive, the most promising research in cognitive training in children with SCD and cancer has been conducted in the area of working memory. Furthermore, working memory training has been shown to lead to changes in brain structures and functions of the front parietal regions, which are critical for working memory (Takeuchi et al., 2011). Consequently, it is crucial to understand how working memory training can best be applied to remediate problems in children with SCD or cancer.

Need for Adaptations to Working Memory Training in Children with SCD and Cancer

Disease Related Adaptations

Children with SCD or cancer face additional challenges to working memory training due to the direct impact of the disease. For example, the variability of the source of cognitive impairment in children with SCD or cancer as well as incremental deficits in cognitive functioning produce a more complex set of cognitive deficits for these children. These cognitive changes that occur may be subtle and more difficult to detect. In addition, children in this population must manage medical concerns that often take priority over cognitive training. Consequently, it is important to understand the disease related factors that may influence cognitive training in children with SCD or cancer in order to develop effective intervention for cognitive deficits.

Source of Cognitive Impairment in Children with Cancer. Treatment for childhood brain tumors and ALL consists of a combination of treatments including cranial radiation therapy (CRT), chemotherapy and surgery (Moore, 2005). CRT appears to be the most detrimental to neurocognitive functioning, with children that have received this treatment scoring the lowest, followed by children receiving intrathecal chemotherapy treatment, and children with no CNS treatment scoring the highest (Moore, Copeland, Ried, & Levy, 1992). Specifically, children that have received CRT tend to show deficits in attention (Dowell, Copeland, Fletcher, & Stovall, 1991; Moore et al., 1992; Mulhern et al., 2004), processing speed (Schatz, Kramer, Albine, & Matthay, 2000), working memory (Dennis, Heterington, & Speigler, 1998; Schatz, et al., 2000), and IQ (Dowell et al., Schatz, et al., 2000). In addition to treatment variables, other factors such as age, gender, (Butler & Copeland, 1993) intensity of treatment (Turner, Rey-Casserly, Liptak, & Chordas, 2009), and tumor location (King et al., 2004) can influence severity of neurocognitive effects.

Source of Cognitive Impairment in Children with Sickle Cell Disease. The most common and most serious source of neurocognitive impairment in children with SCD is overt stroke, which affects approximately 5% of children with SCD (Ohene-Frempong, 1998). Children with SCD are also at risk for silent cerebral infarction or silent stroke, which is characterized by neuroimaging abnormalities consistent with cerebral infarction without physical neurologic symptoms (Adams et al., 2001). Both silent and overt stroke have been linked to neurocognitive complications in children with SCD (Schatz et al., 2001; Vichinsky et al., 2010). Neurocognitive deficits also appear to occur without visible cerebral infarction, including brain oxygenation and/or perfusion deficits (Schatz et al., 2002). Children with SCD also score lower than age-matched peers on measures of academic achievement and IQ, even in the absence of an overt or silent stroke (Schatz et al., 2002; Steen et al., 2005). Specific areas that are affected in children with SCD include attention, concentration, reading decoding (Brown, Buchanan et al., 1993) crystallized ability, processing speed, short-term memory (Schatz, Finke, & Roberts, 2004) and executive skills including working memory (Schatz & Roberts, 2007).

Impact of source of neurocognitive impairment on working memory training. The variability of source of neurocognitive impairment in children with SCD and cancer has implications for outcomes associated with cognitive intervention. This is due to the vast differences in cognitive profiles between two children with the same disease who have working memory deficits. Although some children within these populations have cognitive deficits only in the area of working memory, other children may experience additional cognitive impairment that may influence their ability to show progress on working memory outcome measures. Consequently, it is important to consider how the source of cognitive impairment can lead to differences in neurocognitive profiles and how that may influence cognitive training for each individual in a working memory training program.

Incremental deficits in cognitive functioning. In children with SCD and cancer, cognitive deficits appear to worsen with age, which is in contrast to other conditions such as ADHD, which show improvement in intellectual functioning with age (Coghill, Hayward, Rhodes, Grimmer, & Matthews, 2013; Huang, Wang, & Chen, 2012). For example, a meta-analysis conducted on studies of cognition in SCD found a statistically significant difference in effect sizes for the older children (11-13 year olds) than younger children (9-10 year olds), suggesting a larger discrepancy in cognitive functioning for older children with SCD in comparison to healthy control children (Schatz, Finke, Kellet, & Kramer, 2002). Children with cancer also tend to demonstrate worsening cognitive effects as they age. This is due to evidence that increased time from CRT is associated with worse neurocognitive functioning in children with pediatric cancer (Copeland, deMoor, Moore, & Ater, 1999; Mulhern et al., 2001; Palmer et al., 2001; Palmer et al., 2003). Consequently, brain damage in children with cancer may be delayed until several years after treatment (Brouwers, Riccardi, Fedio, & Poplack, 1985; Brown et al., 1992).

Impact of incremental deficits on working memory training. A decline in cognitive functioning with increasing age has implications for the time in which working memory training occurs. Due to worsening cognitive performance, it appears that acquiring new skills and information becomes more difficult as children age, suggesting that intervention when children are older may become more and more challenging for these children. However, the delay in cognitive deficits in children with cancer and the subtlety of deficits in children with SCD may make it difficult to detect the presence of cognitive decline that would make children eligible for working memory training programs. Therefore, children that would potentially benefit from working memory training may be missed.

Other medical concerns that impact working memory training. In addition to cognitive effects from SCD and cancer, children with these health conditions experience other significant disease effects that impact their quality of life. For example, children with SCD experience pain, fatigue, priapism, hip necrosis, jaundice, and spleen damage (Rees et al., 2010; Wethers, 2000). Children with cancer experience multiple side effects as a result of the disease including bleeding, bruising and severe anemia (Armstrong, 1999) as well as side effects of treatment including hair loss, weight gain or loss, fatigue, constipation, and low blood counts (Copeland et al., 1988). In a study of childhood cancer patients, 75% of children had one or more adverse events including cardiovascular problems, endocrinology complications such as growth hormone deficiency and thyroid disorder, fatigue, fertility issues, obesity, hypertension, seizures, pain, and psychosocial problems. Furthermore, 40% of the cancer survivors in this study had at least one life threatening or disabling event (Geenen et al., 2007). Disease complications and other adverse events may impact the frequency or duration of training if a medical emergency arises and may also result in missed days of school. In addition, children with cancer or SCD may become fatigued by exercises more easily than a typically developing child.

Treatment for SCD or cancer may also interfere with working memory training. For example, children with SCD take a variety of medications to manage their disease including penicillin to reduce infection, analgesic opiates to manage pain episodes, and hydroxyurea to increase fetal hemoglobin for children with more severe forms of the disease (Rees, Williams, & Gladwin, 2010). Remaining adherent to medication regimens is challenging due to barriers such as busy schedules and forgetting to take medication (Witherspoon & Drotar, 2006) and may actually interfere with activates that contribute to quality of life (Barakat, Lutz, Smith-Whitley, & Ohene-Frempong, 2005). In addition, medications to reduce pain have side effects including sedation, nausea and vomiting that can impact the child's ability to complete training (Yale, Nagib, & Guthrie, 2000). Other treatment procedures for children with cancer or SCD including CRT and chemotherapy for children with cancer and chronic transfusions for children with SCD are time consuming and physically draining, possibly preventing children from being able to complete cognitive training procedures.

Environmental Adaptations

Frequent absences in children with SCD and cancer. In addition to disease factors, a diagnosis of a chronic illness is associated with changes in the child's environment, primarily within the school system and family unit. Children with SCD or cancer are at risk for excessive school absences. Children with cancer miss an average of 40 to 60 days of school in the first year after diagnosis, with some children having to repeat the entire school year (Pini, Hugh-Jones, & Gardner, 2012). Children with cancer have lower school attendance than their peers due to treatment and clinic visits (Mancini, 1989). Although children with cancer miss the most school during the year following diagnosis, research shows that this population often has irregular attendance for up to three years following diagnosis and has difficulties catching up to two years later, suggesting that current absences can affect later school performance (Moore et al., 2009). Despite being more likely to repeat a grade and miss school, survivors of non-CNS cancer were similar to peers on most educational and occupational outcomes during the transition from adolescence to emerging adulthood, suggesting that children with cancer are able to overcome the barrier of frequent absences (Gerhardt et al., 2007).

Children with SCD are also at risk for frequent absences, missing an average of 18 days of school a year (Schatz, 2004). Children with SCD may miss school intermittently due to pain episodes treated at home or hospitalizations that last for many days or weeks. In a self-report study of parents of children with SCD aged 5 to 17 years, 28% of children and adolescents had three or more hospitalizations during a two-year time span (Cant Peterson, 2005). In addition, 30% of children with SCD experience pain every day, while 50% experience pain more than half of the days (Smith et al., 2008). Therefore, even when children with SCD are attending school, they are often in pain. Research suggests that children with SCD who miss school are more likely to have special education services and are more likely to be retained (Schatz, 2004).

Impact of frequent absences on working memory training. Missing school impacts the amount of classroom instruction that children receive. Consequently, children are at risk for falling behind due to missed school days. The impact of missing school is even greater for children with working memory deficits. In the context of a working memory-training program, missing school would limit the ability to train exclusively in the classroom setting. In addition, missing school may limit the impact of working memory training if skills learned through working memory training aren't reinforced in the classroom. In addition to missed days of school, one consideration is that many children with SCD and cancer have a 504 or IEP Plan (Brown et al., 1998). Consequently, parents might not be interested in additional educational intervention.

Family factors that could influence working memory training. Parent-child relationships and family functioning are critical for child adaptation to chronic illness (Wallander, Varni, Babani, Banis, & Wilcox, 1988). Children with chronic illness who are able to gain support from family and friends receive psychosocial benefit beyond these relationships. Social support is positively related to physical and mental health in individuals who have suffered a spinal cord injury (Muller, et al., 2012), is associated with increased self-efficacy in individuals with chronic obstructive pulmonary disease (Bonsaksen, Lerdal & Fagermoen, 2012), and is predictive of negative affect in children with cancer (Varni & Katz, 1997). According to Kazak's implementation of Bronfenbrenner's social ecological model applied to childhood chronic illness, the child exists at the center of the circle, with family in the next ring, and social support systems and the healthcare system in the next ring (Kazak, 1989). The model demonstrates that the family is a central component of a chronically ill child's social support network. Furthermore, the quality of family relationships and other family resources such as income and maternal education also influence adaptation to chronic illness (Wallander et al., 1989).

Family functioning in children with cancer. A diagnosis of a serious illness often disrupts the functioning of the family system. While some families are able to adjust to the demands of the illness, many families report disruptions to family functioning as a result of these demands. Families with an adolescent with cancer report a high rate of family functioning difficulties, with many adolescents and parents reporting poor family functioning overall (Alderfer, Navsaria, & Kazak, 2009). In particular, cancer survivors and their parents report communication difficulties, difficulties with emotional expression within the family, and lack of responsibility within the family (Alderfer, Navsaria, & Kazak, 2009).

Difficulties with family functioning may reflect the various changes that occur within the family as a reaction to the child's illness. Both mothers and fathers of children with cancer report more nervousness and fear and a greater responsibility for the family (Sieminska & Greszta, 2008). Families with a child with cancer also report disruption of career, with some families reporting having to give up employment or alter career plans and duties as well as significant financial strain. In one study, 32% of families surveyed experienced poverty as a result of the illness (Sieminska & Greszta, 2008). Treatment status (whether the child is on or off treatment) is an indicator of the level of parenting stress, which can impact family functioning. Parents who report experiencing more frequent stressors, particularly those pertaining to emotional issues, are more likely to report disruptions in family functioning. This is likely due to the amount of emotional resources that are given to the sick child, which diminishes the available resources that the parent can contribute to the overall family (Streisand, Kazak, & Tercyak, 2003).

Despite difficulties reported by families of children with cancer, many families report positive changes as a result of the diagnosis. When faced with the medical, emotional, and financial demands of their child's illness, many families demonstrate increased coherence and stronger marital ties, as well as stronger religious faith. In addition, some families report stronger ties with relatives as well as more time devoted to the family (Sieminska & Greszta, 2008). A supportive and cohesive family relationship characterized by commitment, help, support, and open expression of feelings can protect against maladaptive responses to the stressor of the illness and lead to lower psychological distress, higher social competence and better overall mental health (Fuemmeler, 2003; Rait et al., 1992; Varni, Katz, Colegrove, & Dolgin, 1996). Positive family relationships are not only critical for overall adjustment to a cancer diagnosis but also have a direct relationship with cognitive functioning. Studies demonstrate that poorer cancer survivor processing speed, working memory, verbal memory, and executive function are significantly associated with poorer family functioning which leads to poorer cancer survivor health related quality of life (Hocking et al., 2015).

Family functioning in children with SCD. SCD is an episodic disorder that significantly impacts the family due to the unpredictability of pain episodes (Rolland, 1984). Caring for a child with SCD is a full-time responsibility requiring approximately 1.5 hours per day devoted to SCD related caregiving tasks. There is significant caregiver burden due to the unpredictability of pain crises and the feelings of guilt, inadequacy and emotional distress that a caregiver experiences when seeing their child in pain (Moskowitz et al., 2007). Factors such as level of cohesion and family conflict may further disrupt family functioning in children with SCD. Families with a children with SCD who self-report to be less cohesive have children that exhibit more externalizing and depressive symptoms according to their mothers, and are rated by teachers as more socially impaired (Brown et al., 1993). A study of family functioning in children with chronic health conditions revealed that children with SCD were at the greatest risk of poor family functioning (Herzer et al., 2010). Sources of disruption in family functioning in children with SCD can include medical crises and hospitalizations, which alter the family routine and reduce the amount of time that families are able to spend with one another and tend to each others needs, impacting the quality of family relationships (Mitchell et al., 2007). Family functioning that is conflicted is associated with poor outcomes including increased behavior problems and poor adjustment, and symptoms of depression (Brown & Lambert, 1999; Thompson, 1999; Thompson et al., 2003).

A cohesive family environment is associated with more active coping in children with SCD (Brown et al., 1993; Kliewer & Lewis, 2000; Lutz, Barakat, Smith-Whitley, & Ohene-Frempong, 2004) and can lead to better adaptation to the disease (Burlew et al., 2000). Greater family cohesion and adaptability can also potentially buffer the negative effects of caring for a child with SCD, even when the child has additional concerns such as behavior problems (Ievers, Brown, Lambert, Hsu, & Eckman, 1998). Predictors of positive family functioning include higher SES and higher internal locus of control in primary caregivers. For example, a parent who perceives higher control may be better able to promote a cohesive and organized family system and access supports needed for the family to address disease management in a successful manner (Barakat, Lutz, Nicoloaou, & Lash, 2005). Positive family functioning has an impact not only on the child with SCD, but also siblings of children with SCD. For example, family coping, support, expressiveness and low conflict, are predictive of positive sibling adjustment, even considering the impact of demographic variables and family characteristics (Gold et al., 2008).

Impact of family functioning on working memory training. Chronic illness can significantly disrupt family relationships and patterns leading to poor family functioning. A family that is characterized as conflicted is less equipped to handle tasks and challenges within the family. A working memory training intervention may further disrupt family dynamics, reducing the amount of quality time that members of the family are able to spend with one another. Consequently, families may be reluctant to engage in working memory training. However, families that are able to handle this temporary disruption would likely benefit overall due to the positive impact that working memory training would have on the child with chronic illness.

Parent Functioning in children with cancer and SCD. Parents of children with SCD and cancer report higher rates of parenting stress than parents of healthy children (Barakat, Patterson, Tarazi, & Ely, 2007; Cabizuca et al., 2009). Higher parenting stress in this population may be due to the additional caregiving demands that are required of parents taking care of a child with a chronic health condition. For example, parents of children with cancer participate in medical caregiving which includes tasks such as changing dressings, administering medicines, and responding to the side effects of treatment as well as more complicated procedures including drawing blood from portable catheters and assessing the child's medical status. Parents are also responsible for transporting and accompanying children to frequent medical visits and providing support during medical procedures (Jones, 2006). Parents of SCD also report increased stress at diagnosis in anticipation of the pain and other symptoms that their child will suffer in the future (Rao & Kramer, 1993).

In addition to higher parenting stress, parents of children with SCD and cancer report higher rates of mental health symptoms. Parents of childhood cancer survivors report grater frequency and intensity of mental health symptoms including intrusive thoughts, hypervigilance, and distress at reminders of the diagnosis and treatment (Barakat et al., 1997) and endorse a greater frequency of stressful life events in general, with 25% of parents meeting DSM criteria for PTSD compared to 7% of mothers of healthy children (Brown, Madan-Swain, & Lambert, 2003). Parents of children with SCD also endorse higher rates of distress including symptoms of anxiety and depression, indicating poor adjustment to their child's illness (Thompson, Gil, Burbach, Keith, & Kinney, 1993). Increased mental health concerns may be a result of more negative perceptions about their child's illness as well as higher levels of caregiving burden and poorer quality of life. Salvador and colleagues found that when parents perceive their child's illness as more severe and as interfering more with the child's life, they also experienced higher levels of caregiving burden and poorer quality of life (2015).

Impact of parent functioning on working memory training. Increased parenting stress and mental health concerns may influence the parent's ability to support their child during working memory training. If parents have increased stress, adding a task of daily training to their schedule may hinder parents from wanting to participate in a working memory training intervention. Even when parents decide to allow their child to participate, they may have trouble completing the sessions. In addition to stress related to the disease, parents of children with SCD and cancer tend to have more contact with the educational system (Kratz et al., 2009) due to increased absences and higher rates of special education and repeating a grade (Pini, Hugh-Jones, & Gardner, 2012; Schatz, 2004), which may add to parenting stress. However, more frequent contact with the school may also help parents to better understand how an educational intervention would benefit their child in achieving academic goals.

Current Study

Cognitive training methods are an innovative avenue to improve working memory among children who have suffered cognitive deficits related to chronic illness. Most studies of cognitive training programs are tailored toward the specific needs of individual illness populations, however, a more generalized program focused on symptoms and level of impairment would reach more children with working memory deficits and use resources more efficiently. According to Sherr and Langenbahn, level of impairment and symptoms are more important than diagnosis when determining cognitive retraining program techniques (1992). In addition, in a study of patients with brain injury, stroke, or other neurological conditions, Stringer found that cognitive retraining was successful regardless of illness severity and across diagnostic groups (2011). Finally, most children followed for a diagnosis of SCD or cancer attend the same Hematology/Oncology clinic, so a program that fits the needs of both populations would be beneficial. Consequently, the current study will include both children with cancer and SCD who demonstrate impairment on measures of working memory.

Children with SCD or cancer are a unique population that requires special consideration before adapting interventions to meet their needs. Due to the impact of the disease and treatment on cognitive functioning and quality of life as well as the changes to the child's family and school environment as a result of the diagnosis, these children may not demonstrate the same benefit from working memory training interventions unless adaptations are carefully considered and implemented. Consequently, additional environmental adaptations will be implemented in order to support these children and families to complete the program. Specifically, working memory training will be offered exclusively over the summer. This adaptation will provide patients with a structured method of engaging in cognitive tasks during the summer and allow more flexibility in training, possibly improving adherence to the program. Summer programs designed to improve school readiness and reading skills in preschoolers through school age children have demonstrated statistically significant improvement and high parent satisfaction with the programs (Graham, McNamara, & Lankveld, 2011; Graziano, Slavec, Hart, Garcia, & Pelham, 2014; Mitchell & Begeny, 2014). In addition, due to evidence that parent involvement in interventions is particularly beneficial for children with cancer or SCD, adjustments will be made to include the parent as a more central component of the training.

A meta-analysis of working memory training in children and adults shows that although working memory training leads to short-term improvements in working memory skills, these improvements do not generalize to other cognitive skills (Melby-Lervag, 2013). Consequently, children that improve working memory skills through working memory training may not show improvement in the classroom setting. Previous studies have investigated whether working memory training translates to improved classroom working memory functioning using classroom analogues of activities that task working memory including following instructions, detecting rhymes, and sentence counting and recall. Although one study of a program that targeted strategy training led to improvements in classroom performance another study using computerized adaptive working memory training did not demonstrate any gains in classroom performance (Dunning, Holmes, & Gathercole, 2013; St. Clair Thompson, 2010). Due to differences in findings in this area and questions related to generalizability of working memory training, this study will use a measure correlated with functional attention performance as well as teacher ratings of working memory to determine the impact of working memory training in the classroom. The specific aims of this study include:

Aim 1) Assess the feasibility of a summer cognitive retraining program for children experiencing working memory deficits in relation to a diagnosis of SCD and cancer.

> Hypothesis 1a: Average adherence will exceed 80% of total sessions.
>
> Hypothesis 1b: Parents will rate the intervention as feasible as defined by mean ratings above 3 on the feasibility measure, adapted from the Program Feasibility Questionnaire.

Aim 2) Measure the effect size of working memory training to remediate impairment in children with SCD and cancer.

> Hypothesis 2a: Children with working memory problems in the intervention who have adhered to the training sessions (completed at least 24 sessions) will improve from baseline to post intervention on the working memory index of the WISC-V.

Aim 3) Determine the generalizability of improvements gained through computerized working memory training to classroom functioning in children with SCD or cancer.

> Hypothesis 3a: Children who have adhered to the intervention will demonstrate improved functional ability from baseline to post intervention on an objective measure correlated with functional attention performance.

Hypothesis 3b: Exploratory analyses will examine a new rating scale of classroom behavioral symptoms of working memory problems to assess its utility for future studies of working memory training.

CHAPTER 2

METHODS

Study Design

The study is a repeated measures, quasi experimental design without a control group.

Subjects

A total of 23 school-age children (ages 7-17) with cancer (brain tumors and Acute Lymphoblastic Leukemia, ALL) or SCD were recruited from a children's hospital in the southeastern United States. In order to be eligible for the program, children had to score one or more standard deviations below the mean on measures of working memory or score in the clinically significant range on the Metacognition Scale of the parent version of the BRIEF. Participants also had to demonstrate intellectual functioning sufficient to understand the training tasks (IQ $\geq$ 70). Children with cancer had to be off treatment for one year prior to participating in the study. Exclusion criteria were a diagnosis of severe conduct disorder, children without internet access, and non English-speaking children. Approximately 40 children were determined to be eligible to participate according to their diagnosis, presence of working memory concerns, and an appointment date within the study time frame. Out of 23 children interested in participating, 17 children ages 7-17 with a diagnosis of SCD (n = 14) or cancer (n = 3) were eligible to complete the study.

Intervention Procedures

Children diagnosed with cancer or SCD were identified through chart reviews. Patients who were eligible due to their diagnosis were approached at their clinic appointment or received a letter or phone call describing a program designed to improve working memory problems in children. Following recruitment, parents and children completed baseline measures including informed consent and assent, a parent interview, working memory measures, a measure of intelligence, a measure of attention, and a demographic questionnaire. Families approached at their clinic appointment could choose to complete baseline measures at that time or may have scheduled an additional appointment to complete baseline measures. Following completion of baseline measures, teachers completed a measure of executive functioning and a measure of working memory based on Dehn's model of working memory classroom observation (Dehn, 2008). Families were then able to select their start date during the summer break in which their child would participate in 6 weeks of training for 30 to 40 minutes per day for a total of 30 sessions using Cogmed Robo Memo cognitive training.

Training aids (graduate clinical psychology students) offered technical assistance and engaged in weekly coaching sessions over the phone. The weekly coaching sessions took place at the beginning of the training week and allowed the coach to highlight successes, provide support and encouragement, and answer any questions. Incentives were given to children for each session completed. Children were tested as close to one month following the intervention; however, due to scheduling problems the range of values was one to five months. Children and parents completed post intervention measures at the hematology/oncology clinic including working memory measures and a feasibility questionnaire. In addition, teachers completed follow-up measures of executive functioning and working memory. See table 2.1 for a complete timeline of measures and figure 2.1 for a full consort diagram.

Assessments and Measures

Baseline Measures. The *Behavior Rating Inventory of Executive Functioning (BRIEF)* is an 86-item questionnaire measuring executive functioning in children 5-18 through parent and teacher report. The inventory includes eight subscales, which are grouped into two indexes and one summary score. The metacognition index was used for this study and includes the Initiate, Working Memory, Plan/Organize, Organization of Material and Monitor subscales. The Global Executive composite (GEC) was also used to report a summary score based on all eight scales. The BRIEF has been used previously in studies assessing working memory training (Beck et al., 2010; Egeland, Aarlien, & Saunes, 2013). The *Demographic Questionnaire* contains questions assessing basic background information of participants. The entire measure can be found in appendix C. The *Parent Interview* includes questions used to assess parent motivation and preferences for working memory training. The aim of the questionnaire is to increase parent motivation and involvement in working memory training and provide parents with choices for conducting the training. The entire measure can be found in appendix B.

Primary Outcome Measures, Hypothesis 1. *CogMed RoboMemo (RM)* is a computerized visuo-spatial and verbal working memory training program designed for school age children ages 7 and up. There are a total of 12 exercises, although children are only required to complete 8 exercises per day. Within each exercise, there are 15 trials for a total of 120 trials per day. It typically takes children 30-40 minutes per day to complete the training. The 6-week, 30 session protocol was used for this study. The *Summer Working Memory Training Feasibility Questionnaire* was developed based on the Program Feasibility Questionnaire developed by Kronenberger and colleagues and adapted to meet the needs of this study. Specifically, the following questions were added in order to assess feasibility during the summer: “Training during the summer was convenient” and “Training during the summer allowed flexibility with our family schedule” and will be used as the primary outcome questions. “My child thought that the exercises were fun” and “My child became frustrated with the exercises” were also added based on questions included in other feasibility studies using working memory training. Questions that weren’t relevant to the study were eliminated. The entire questionnaire can be found in Appendix D.

Exploratory Outcome Measure, Hypothesis 1. The *Summer Working Memory Training Feasibility Questionnaire-Child Version* was modified from the parent version of the same measure to be developmentally appropriate for children. The entire questionnaire can be found in the appendix.

Primary Outcome Measure, Hypothesis 2. The *Wechsler Intelligence scales for children, fifth edition (WISC-V)* is an individually administered clinical instrument for assessing the cognitive ability of children aged 6 years 0 months through 16 years 11 months. The WISC-V provides subtest and composite scores that represent intellectual functioning in specific cognitive domains. For the purposes of this study, the Verbal Comprehension and Matrix Reasoning subtests were used to determine that participants had the necessary cognitive functioning to complete the intervention (IQ≥70). In addition, the Digit Span, Picture Span, and Letter-Number Sequencing subtests were administered in order to yield a Working Memory Factor score.

Primary Outcome Measure, Hypothesis 3. The *Test of Everyday Attention for Children (TEA-Ch)* is designed to measure selective, sustained attention, and attentional switching in children ages 6-16. This measure includes nine subtests: *Sky Search, Score!*, *Code Transmission*, *Creature Counting, Sky Search-Dual Task, Map Mission, Score!-Dual Task, Walk/Don't Walk* and *Opposite World.* and is significantly correlated with school performance (Manly et al., 2001). Three tasks were chosen to assess the generalization of working memory training to executive attention tasks that have working memory components: *Creature Counting, Score! - Dual Task, and Opposite World*. Creature Counting is a measure of attentional control/switching. In this task, children are asked to count aliens in their burrow, switching between counting upwards and counting downwards. Time taken and accuracy are scored in this subtest. Score! - Dual Task measures sustained attention. In this task, children are asked to count scoring sounds. As they count, they also have to listen for an animal name during a spoken news report. A total score is obtained from the number of accurate sounds counted and animals identified. The Opposite World task is part of the attention control/switching factor and has predominant demands on inhibiting automatic responses. In the same world condition, children follow a path naming the digits 1 and 2. In the Opposite World they do the same task except this time they have to say "one" when they see a 2 and "two" when they see a 1. In both tasks, the speed with which the children can perform this cognitive reversal is scored.

Exploratory Outcome Measure, Hypothesis 3. The *Teacher Working Memory Checklist* is a measure based on Dehn's model of working memory classroom observation. The checklist assesses working memory in a variety of domains including general working memory, phonological short-term memory, visuospatial working memory, verbal working memory, and executive working memory in order to assess functioning in the classroom. The entire measure can be found in appendix A.

Data Analysis

For Aim 1, hypothesis 1a, the percentage of children with at least 80% adherence (24 sessions) was computed. For Aim 1, hypothesis 1b, mean ratings of scores for questions related to summer training on the feasibility measure were computed in order to detect a statistically significant difference in means, $H_0 = 3.0$, $H_1 = 3.6$. Power estimates indicated that I would have 80% statistical power to detect a medium effect (0.6) with alpha = 0.5 and n = 19. For Aim 2, the Cogmed index improvement was calculated for children that completed the program. Repeated measures ANOVA was used to measure the effect size of changes in working memory between baseline and post intervention. For Aim 3, scores on the TEA-Ch were compared from baseline to post intervention using a t-test.

Table 2.1. Measurement Procedures

Visit	**Duration**	**Measures**	
1) Baseline Measures	1.5 hours	Demographic Questionnaire	Parent BRIEF
		Informed consent/assent	WISC-V
		Parent Interview	TEA-Ch
2) Baseline Teacher Measures	1 hour	Teacher Working Memory Checklist	
		Teacher BRIEF	
3) Working Memory Training	35 min a day for 6 weeks	CogMed Robo Memo	
4) Follow Up Measures	1.5 hours	Feasibility Questionnaire- Parent	Parent BRIEF
		TEA-Ch	WISC-V
5) Posttest Teacher Measures	1 hour	Teacher Working Memory Checklist	
		Teacher BRIEF	

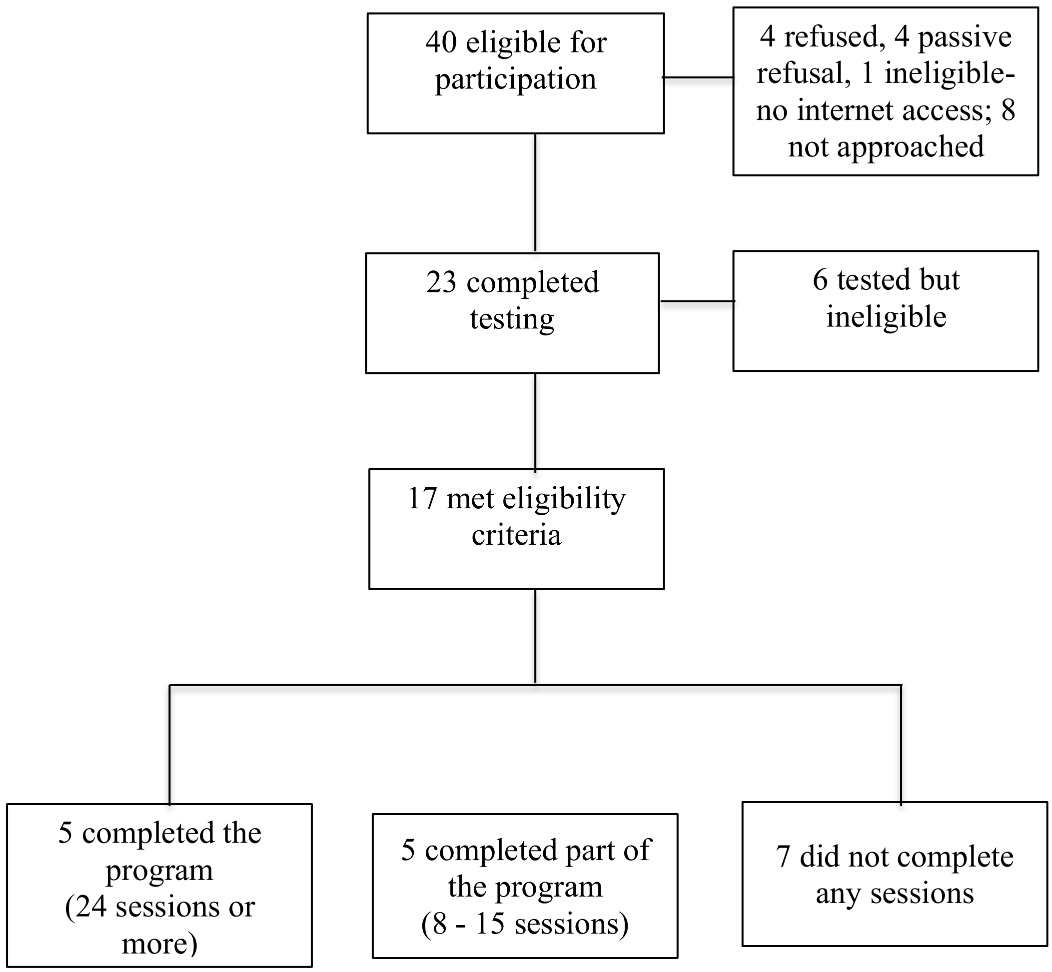

Figure 2.1 Consort Diagram

CHAPTER 3

RESULTS

Aim 1, Hypothesis 1a

For Hypothesis 1a of Aim 1, analyses were conducted to determine the average adherence for the sample. The results indicated that only 29.4% of participants completed the full program, with 58.8% completing at least 8 sessions. Of the 17 children that participated in the study, 5 children completed the program (29.4%), 5 children completed between 8 and 15 sessions (29.4%), and 7 children did not complete any sessions (41.2%).

Additional descriptive statistics were examined to determine if there were any potential predictors of participants that completed versus participants that did not complete the full program. Children that completed the full program completed sessions ranging from 7 weeks to 18 weeks with an average of 12 weeks. Children that completed the full program ranged in age from 7 to 14 years, including 3 males and 2 females. Full completers were equally distributed across diagnosis groups, with 3 children with SCD and 2 children with a brain tumor completing the full program. Children that completed the program were also equally distributed across SES backgrounds (SES ranging from less than $10,00 to over $90,000). All completers had parents that completed at least some college education. Conversely, partial completers and non-completers tended to report lower levels of income than completers despite similar levels of education. For example 60% of partial completers and over 70% of non-completers reported a total household income of less than $30,000 a year.   In addition, all of the participants that did not complete the program had a diagnosis of SCD. See Table 3.1 for a full list of demographic characteristics by group.

Aim 1, Hypothesis 1b

For Aim 1, Hypothesis 1b, analyses were conducted to determine the feasibility of implementing a summer working memory training program in this population. An independent samples t-test was conducted to compare scores on the parent feasibility measure from H_0 (see table 3.2). For the primary outcome questions, a significant difference was found for the item, “training during the summer was convenient”, $t(8) = 2.63$, $p = .03$, such that the majority of parents agreed with this statement (77.8%). There was also a significant difference found for the item “training during the summer allowed flexibility”, $t(8) = 5.66$, $p = .00$. However, only 44.4% agreed with this item while 44.4% disagreed. Further exploratory analyses revealed that a significant difference was also found for the items, “my child’s working memory improved after Cogmed”, $t(8)$, = 3.50, $p = .01$ (66.7% agreed), “my child’s learning ability improved after Cogmed”, $t(8) = 2.87$, $p = .02$ (77.8% agreed), “I was happy with the results of Cogmed”, $t(8) = 5.50$, $p = .00$ (88.9% agreed), and “I would recommend Cogmed to others”, $t(8) = 8.22$, $p = .00$ (100% agreed). However, there was also a significant difference found for the items “a lot of child effort was required for Cogmed”, $t(8) = 4.40$, $p = .00$ (77.7% agreed) and “A lot of parent effort was required for Cogmed”, $t(8) = 4.24$, p = .00 (77.8% agreed). For child feasibility ratings, we calculated the percentage of children that agreed with each of the statements. Please see table 3.3 for child feasibility ratings.

Aim 2

For Aim 2, analyses were conducted to understand the efficacy of the intervention by examining changes from baseline to time 2. To describe practice effects on the training task, I compared completers to partial completers on the Cogmed index of improvement. The mean Cogmed index improvement was 33.2 (SD = 12.56) for completers and 24.6 (SD = 16.6) for partial completers. A paired samples t-test revealed that the improvement was significant for completers $t(4) = -5.91$, $p = .00$; d = 1.65 and partial completers $t(4) = -3.31$, $p = .03$, d = 1.50.

For the comparison of pre-post working memory outcomes using a repeated measures analysis of variance (ANOVA) procedure the dependent variable was WISC-V Working Memory Composite Score and the independent variables were time (pre-training, post-training) and group (completers, partial completers, non-completers). The analysis did not indicate statistically significant differences between groups, $F(2) = .31$, $p = .74$, d = .05. This same procedure was conducted with each WISC-V working memory subtest as the dependent variable. The results did not indicate a significant difference between groups on the Letter-Number Sequencing subtest of the WISC, $F(2) = 1.07$, $p = .38$, d = .16, the Digit Span subtest, $F(2) = .95$, $p = .42$; d = .15, or Picture Span subtest, $F(2) = .11$, $p = .90$; d = .02. Due to the small sample size, descriptive comparisons of mean scores from time 1 to time 2 for each group were examined.

Follow-up analyses using a paired samples t-test to examine pre-post effects within each group indicated a non-significant improvement in group means on the WISC-V Working Memory Composite Score for all groups. However, changes in group means showed a large effect size for completers, $t(4) = -1.66$, $p = .17$, d = .87 and a medium effect for partial completers, $t(4) = -.62$, $p = .57$, d = .37. Conversely, group means for the Working Memory Composite showed only a small effect for non-completers, $t(3) = -.34$, $p = .76$, d = .10. A paired samples t-test was also computed to measure improvements in each working memory subtest from time 1 to time 2. The results for completers indicated a large effect size for improvements in scaled score group means for the Digit Span, $t(4) = -1.66$, $p = .17$, d = 1.2 and Letter-Number Sequencing subtests, $t(4) = -2.45$, $p = .70$, d = .90, but only a small effect for the Picture Span subtest, $t(4) = .59$, $p = .59$, d = .26. A similar large effect size was found for the partial completers on Digit Span, $t(4) = -3.09$, $p = .04$, d = .87 and a medium effect for Letter-Number Sequencing, $t(4) = .83$, $p = .46$, d = .43, while Picture Span demonstrated only a small effect, $t(4) = .30$, $p = .78$, d = .24. Changes in mean scores for non- completers showed a small effect for all three subtests (Digit Span, $t(3) = -.55$, $p = .63$, d = .03; Letter-Number Sequencing, $t(3) = -.78$, $p = .50$, d = .06; Picture Span, $t(3) = .5$, $p = .64$, d = .31). See Tables 3.4 and 3.5 for baseline and follow up scores as well as figures 3.1 through 3.4 of graphical depictions of results.

Aim 3

For Aim 3, analyses were conducted to determine how well improvements in working memory generalized to functional attention performance. Mean scores for each subtest of the TEA-Ch were examined to look for improvements from time 1 to time 2. In addition, a t-test was conducted to determine whether this improvement was statistically significant and effect size was calculated for each subtest. The absolute value of scores was higher at post-treatment than pre-treatment for all subtests of the TEA-CH for participants who completed the full program, but were not statistically significant. However, a medium to large effect size was found for a few of the subtests. A large effect was found for Creature Counting Total Correct, $t(4) = 1.29$, $p = .27$, d = .87 and Same World $t(4) = -1.91$, $p = .13$, d = .80, while a medium effect was observed for Opposite World, $t(4) = -2.14$, $p = .10$, d = .55. However, Creature Counting Timing, $t(4) = -1.63$, $p = .18$, d = .34 and Score DT, $t(4) = -.31$, $p = .77$, d = .22 showed only a small effect.

For partial completers, scores on the TEA-Ch showed a large effect for the Creature Counting Total Score, $t(4) = -1.28$, $p = .27$, d = 1.08, a medium effect for Opposite World, $t(4) = -1.4$, $p = .23$, d = .39, and a small to no effect for the remaining subtests (Creature Counting Timing, $t(4) = -.49$, $p = .65$, d = .17; Score DT, $t(4) = .00$, $p = 1.00$, d = 0; Same World, $t(4) = -.49$, $p = .65$, d = .27.

T-tests for non-completers were run with data from four participants who completed time 1 and time 2 measures. Changes in mean scores showed a large effect for Creature Counting Total Correct, $t(3) = -1.71$, $p = .19$, d = .84 and a medium effect for Opposite World, $t(3) = -2.33$, $p = .10$, d = .56. Changes from time 1 to time 2 for Same World showed a small effect, $t(3) = -2.61$, $p = .08$, d = .28 and no effect was found for Score DT, $t(3) = 0.00$, $p = 1.00$, d = 0.00. Creature Counting Timing showed a medium effect, $t(1) = 1.00$, $p = .50$, d = .56, but represents a decrease in scores from time 1 to time 2. This t-test should be interpreted with caution as the Creature Counting Timing score could only be calculated for 2 out of 4 participants due to their inability to obtain a score of 3 or more on the Creature Counting Total Correct Score. Of note is that scores for non-completers were lower than those of completers and partial completers at baseline on all subtests of the TEA-Ch. Please refer to tables 3.4 and 3.5 for baseline and follow up scores as well as figures 3.1 through 3.9 for graphical depictions of changes in TEA-Ch scores from time 1 to time 2.

Exploratory analyses were conducted using the Working Memory Checklist to assess items that may be most helpful in future scale development. For each student, the primary classroom teacher completed the questionnaire for students in first through fifth grade. Middle school and high school students were asked to select the teacher that knows them best. Out of 17 participants, 14 teachers filled out the questionnaires and returned them to the research team at time 1. Out of 50 items, 11 were rated as sometimes or always a problem in over 70% of the sample. An additional 16 items were rated as sometimes or always a problem in over 50% of the sample (see Table 3.6). In addition, a Pearson correlation was conducted to determine how well the Working Memory Checklist correlates with the Working Memory subscale of the Teacher BRIEF. At baseline, the Teacher BRIEF working memory subscale correlated with "has difficulty staying focused during cognitively demanding activities but attends well when cognitive demands are minimal", "fails to complete complex activities" ,"has difficulty keeping track of place during challenging activities", "has difficulty integrating new information with prior knowledge", "has difficulty remembering multistep oral directions", "has more difficulty remembering digits than words", "does not notice the signs during arithmetic calculation", "has difficulty taking meaningful notes", "answers to oral comprehension questions are off-topic or irrelevant (has difficulty inhibiting irrelevant information", "inaccurately estimates memory performance before, during, and after a task", "does not use learning strategies or does not use them on a consistent basis", "does not use the most basic strategies, such as subvocal rehearsal (i.e., inner speech during silent reading)" and "selects inefficient strategies during problem solving". In order to determine the influence of outliers, the cases with the highest and lowest scores on the working memory checklist and the BRIEF working memory subscale were eliminated from the data and correlations were rerun. Without outliers, the analyses indicated that the BRIEF working memory subscale did not correlate with any items on the working memory checklist. See table 3.9.

Table 3.1. *Demographic Characteristics by Group*

Variable	Completers (n = 5)	Partial Completers (n = 5)	Non-Completers (n = 7)
Age (M, SD)	11.8 (2.9)	12.4 (1.8)	11.1 (4.1)
Gender (Male)	3 (60%)	3 (60%)	2 (28.6%)
Diagnosis (SCD	3 (60%)	4 (80%)	7 (100%)
Race (African American)	3 (60%)	5 (100%)	7 (100%)
Family Income			
Less than $10,000	1 (20%)	1 (20%)	2 (28.6%)
$10,000 – $19,000	0 (0%)	1 (20%)	0 (0%)
$20,000 - $29,000	1 (20%)	1 (20%)	3 (42.9%)
$30,000 - $39,000	0 (0%)	2 (40%)	0 (0%)
$40,000 - $49,000	1 (20%)	0 (0%)	2 (28.6%)
$50,000 - $59,000	1 (20%)	0 (0%)	0 (0%)
Over $60,000	1 (20%)	0 (0%)	0 (0%)
Parent Education			
High School Graduate	0 (0%)	1 (20%)	1 (14.3%)
Some College	1 (20%)	2 (40%)	2 (28.6%)
Associates Degree	1 (20%)	1 (20%)	4 (57.1%)
Bachelor’s Degree	3 (60%)	0 (0%)	0 (0%)
Master’s Degree	0 (0%)	1 (20%)	0 (0%)

Table 3.2. *Parent Feasibility Ratings*

Variable (n = 8)	**M**	***t*(8)**	**%Agree**	**%Disagree**
Training during the summer was convenient.	4.1*	2.63	77.8	22.2
Training during the summer allowed flexibility.	4.3*	5.66	44.4	44.4
Difficult to do during the first week.	3.2	.80	44.4	22.2
Difficult to do during the last week.	3.4	1.08	55.5	33.3
Difficulty motivating child during the first week.	3.3	.71	55.5	33.3
Difficulty motivating child during the last week.	3.2	.56	33.3	33.3
My child thought that the exercises were fun.	3.2	.80	44.4	22.2
My child became frustrated with the exercises.	3.6	1.89	55.5	11.1
My child's working memory improved after Cogmed.	3.8*	3.50	66.7	0.0
My child's learning ability improved after Cogmed.	3.9*	2.87	77.8	11.1
I was happy with the results of Cogmed.	4.2*	5.50	88.9	0.0
A lot of child effort was required for Cogmed.	4.2*	4.40	77.7	0.0
A lot of parent effort was required for Cogmed.	4.0*	4.24	77.8	0.0
I would recommend Cogmed to others.	4.4*	8.22	100	0.0

Notes: Scale 1-5 from strongly disagree (1) to strongly agree (5). T-tests were run to determine if each value differed significantly from a value of 3.0. $*p < .05$

Table 3.3. *Child Feasibility Ratings*

Variable (n = 10)	%Agree	% Neutral	% Disagree
It was easier to use the computer program during the summer rather than during the school year.	50	40	10
I liked being able to use the program when I wanted throughout the day rather than after school.	60	40	0
The computer program was easy to use.	60	30	10
I felt like playing the computer program most of the time.	20	30	50
I thought that the computer program was fun.	22.2	44.4	33.3
Playing the computer program made me frustrated (angry).	40	60	0
Playing the computer program helped me do better in school.	50	30	20
I would tell other kids to use this computer program.	30	50	20

Table 3.4. *Baseline Scores*

Variable *M* (SD)	Completers (n = 5)	Partial Completers (n = 5)	Non-Completers (n = 7)	F	*p*
Baseline IQ Composite Score	86.4 (10.8)	94.8 (20.0)	86.7 (12.0)	.57	.58
WISC-V WM Composite Score	85.6 (5.4)	83.2 (3.4)	84.4 (9.5)	.14	.87
WISC-V Digit Span SS	7.2 (1.1)	6.0 (1.9)	6.4 (2.0)	.61	.56
WISC-V Picture Span SS	8.0 (1.0)	8.4 (1.5)	8.3 (2.4)	.06	.94
WISC-V Letter Number Sequencing SS	8.0 (1.0)	8.6 (2.4)	6.6 (2.5)	1.4	.27
TEA-Ch Creature Counting Total Correct SS	8.4 (2.7)	8.6 (3.2)	5.4 (1.7)	3.1	.08
TEA-Ch Creature Counting Timing SS	6.4 (3.2)	6.6 (2.1)	5.8 (2.9)	.11	.90
TEA-Ch Score-DT SS	8.4 (3.2)	6.2 (4.1)	6.1 (2.5)	.84	.45
TEA-Ch Same World SS	5.4 (2.6)	5.6 (0.9)	4.9 (3.1)	.15	.87
TEA-Ch Opposite World SS	5.4 (2.5)	5.8 (2.6)	4.4 (2.7)	.44	.65

Table 3.5. *Follow Up Scores*

Variable *M* (SD)	M (SD) Completers (n = 5)	M (SD) Partial Completers (n = 5)	M (SD) Non-Completers (n =4)	F	*p*
WISC-V WM Composite Score	95.2 (14.7)	87.2 (14.7)	86.3 (24.1)	.31	.74
WISC-V Digit Span SS	10.6 (3.7)	7.8 (2.2)	7.5 (4.7)	.95	.42
WISC-V Picture Span SS	7.6 (1.9)	7.8 (3.2)	7.3 (3.8)	.11	.90
WISC-V Letter Number Sequencing SS	9.2 (1.6)	7.8 (1.1)	6.8 (3.9)	1.1	.38
TEA-Ch Creature Counting Total Correct SS	10.8 (2.8)	11.8 (2.7)	8.0 (2.8)	2.2	.16
TEA-Ch Creature Counting Timing SS	7.6 (3.9)	7.0 (2.5)	6.5 (3.5)	.06	.95
TEA-Ch Score-DT SS	9.0 (2.0)	6.2 (2.6)	6.0 (3.5)	1.9	.20
TEA-Ch Same World SS	7.4 (2.4)	6.0 (1.9)	6.0 (4.4)	.36	.70
TEA-Ch Opposite World SS	7.0 (3.3)	6.8 (2.5)	5.3 (3.4)	.42	.69

Notes: Three of the CogMed non-completers also did not complete follow-up testing.

Table 3.6. *Working Memory Checklist Frequently Endorsed Items and Correlation with Teacher BRIEF Working Memory Subscale*

Question	*p*
General	
Classroom performance is poorer than predicted from standardized scores	.19
Difficulty staying focused during cognitively demanding activities	*.01
Prefers to simplify tasks whenever possible	.18
Fails to complete complex activities	*.00
Difficulty keeping track of place during challenging activities	*.01
Difficulty retrieving information when engaged in another processing task	.21
Difficulty integrating new information with prior knowledge	*.05
Rarely contributes to class discussions	.72
Makes comments such as, “I forget everything”.	.24
Difficulty organizing information during written expression	.16
Difficulty retaining partial solutions during mental arithmetic	.25
Difficulty memorizing and retaining facts	.41
Is very slow at arithmetic computation	.15
Phonological Short-Term Memory	
Difficulty remembering multistep oral directions	*.02
Difficulty blending phonemes into words when reading	.60
Difficulty with phonetic decoding of text (i.e. sounding out words)	.89
Difficulty with phonetic recoding (spelling).	.93
Difficulty learning new vocabulary.	.74
Difficulty producing complex sentences.	.52
Verbal Working Memory	
Requires frequent reminders.	.15
When called on, forgets what was planning to say.	.47
Forgets the content of instruction.	.06
Difficulty paraphrasing spoken information.	.18
Difficulty taking meaningful notes.	*.05
In 3rd grade and above, continues to finger count during arithmetic calculation.	.77
Rereads text when there has not been a decoding problem.	.33
Difficulty remembering the first part of sentence or paragraph when reading.	.71
Produces only short sentences during written expression.	.06
Has frequent subject-verb agreement in written expression.	.79
Omits some of the content when writing a sentence.	.52
Executive Working Memory	
Difficulty switching between operations	.12
Difficulty taking notes and listening at the same time	.11
Does not use learning strategies or does not use them on a consistent basis	*.01
Prefers to use simple instead of complex learning strategies	.35
Selects inefficient strategies during problem solving	*.01

*Table includes only items endorsed as problematic for at least 50% of the sample

Figure 3.1. Working Memory Index by Group

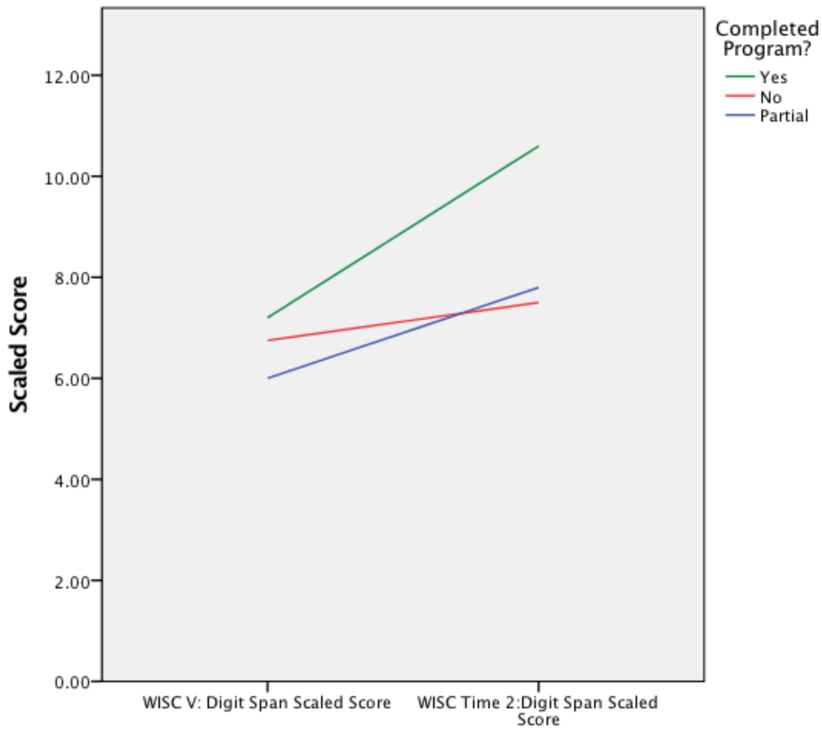

Figure 3.2 Digit Span Scores by Group

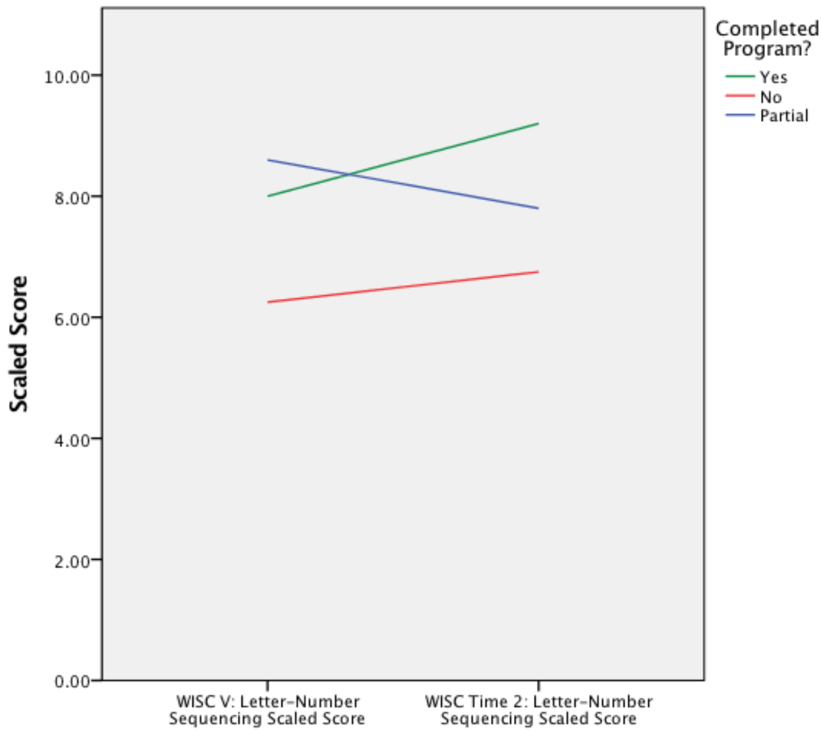

Figure 3.3 Letter-Number Sequencing Scores by Group

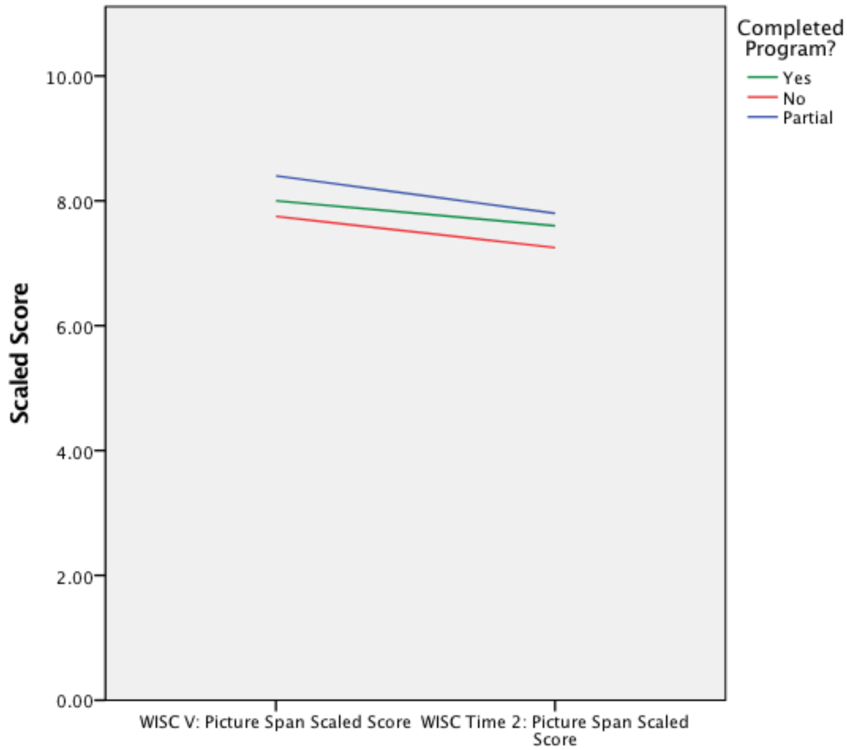

Figure 3.4 Picture Span Scores by Group

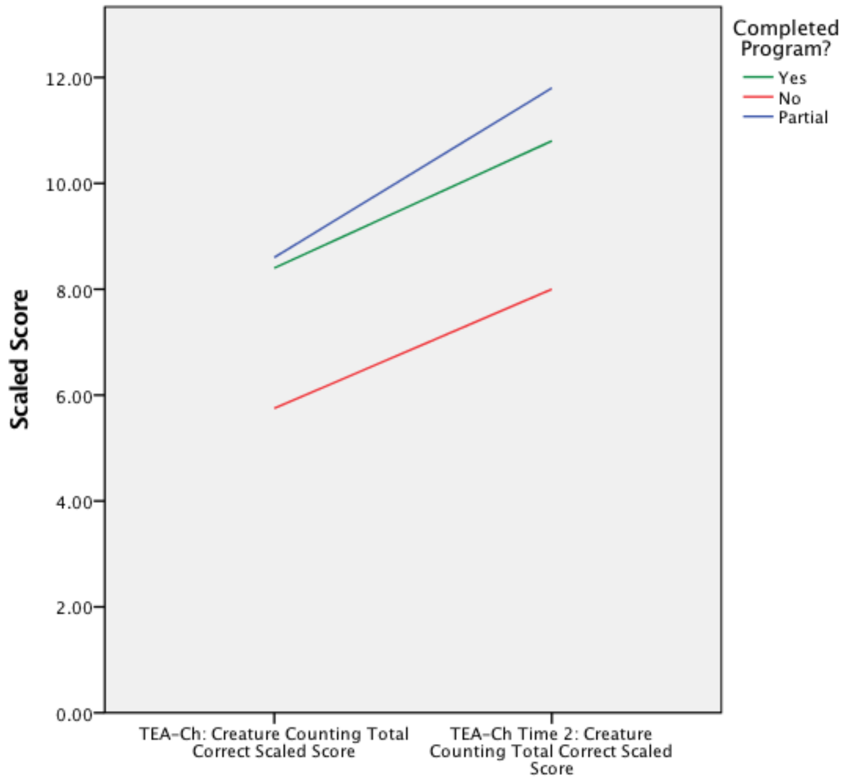

Figure 3.5 Creature Counting Total Correct by Group

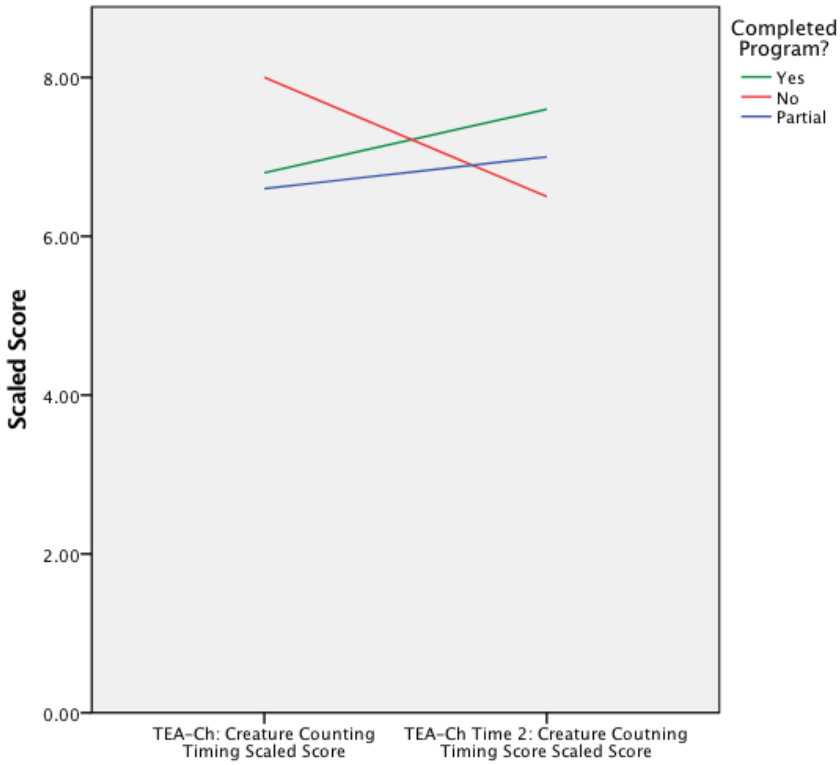

Figure 3.6 Creature Counting Timing Score by Group

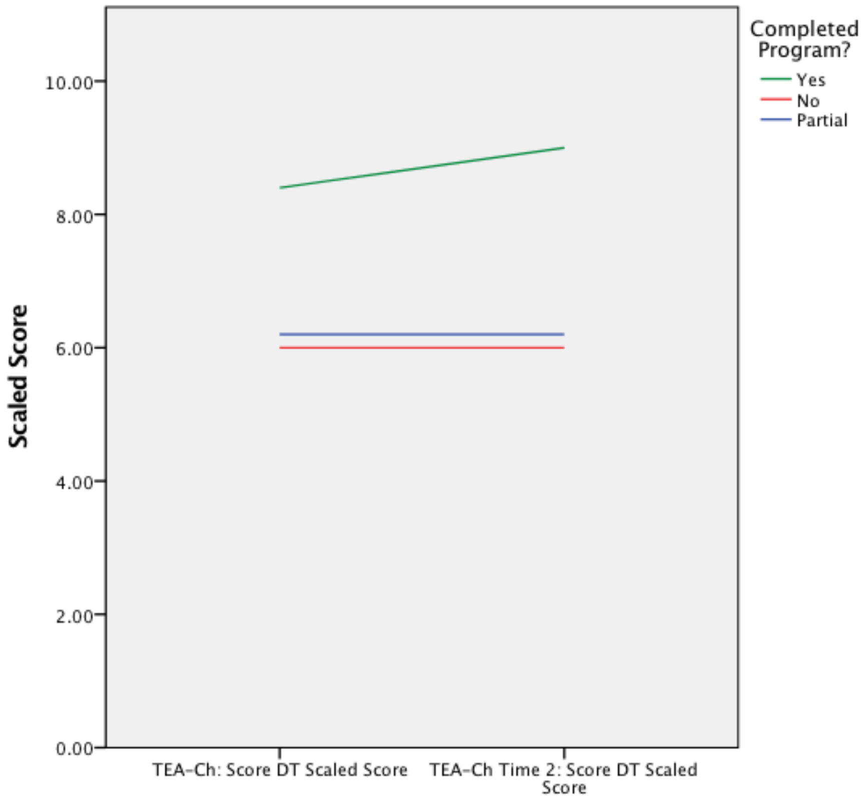

Figure 3.7 Score DT by Group

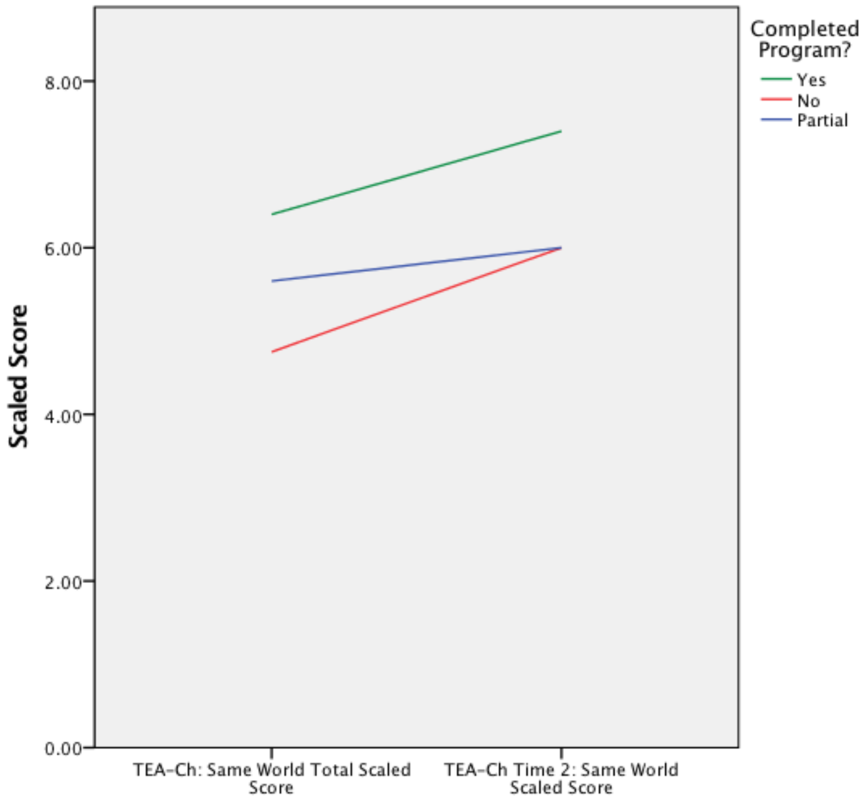

Figure 3.8 Same World by Group

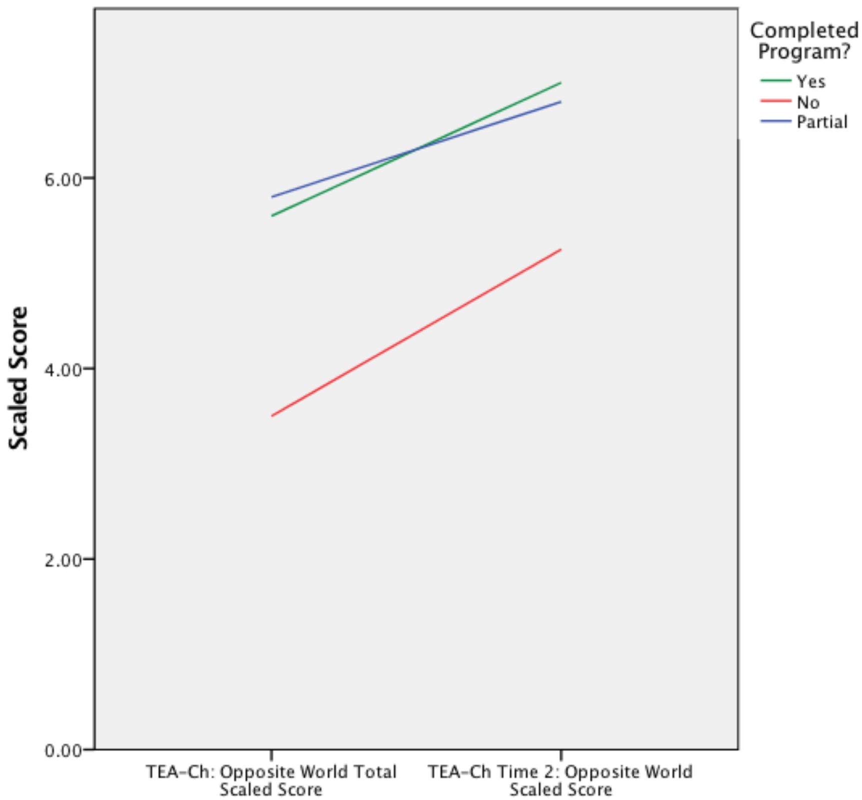

Figure 3.9 Opposite World by Group

CHAPTER 4

DISCUSSION

Previous studies suggest that computerized cognitive remediation programs are effective for children with chronic health conditions (Conklin et al., 2015; Hardy et al., 2013; Hardy et al., 2016; Hardy, Willard, & Bonner, 2011). However, disease complications and treatment can affect adherence to cognitive training, reducing the benefit of the intervention. In addition, it is unclear the extent to which gains in working memory translate to improvements in everyday settings such as improved classroom functioning. In this study, a working memory training program was conducted to examine the impact of delivery modifications (e.g., delivering the intervention exclusively over the summer) on feasibility, efficacy, and generalizability to the classroom setting in children with SCD and cancer. Contrary to Hypothesis 1a, that adherence rates would exceed 80%, the results indicated that only 29.4% of participants completed the full program, with 58.8% completing at least 8 sessions. Participants who were adherent to the full program trained over a longer period of time than expected by the Cogmed protocol. Despite the additional time available during the summer to train, even participants who were able to complete the program did not complete sessions within the prescribed 6-week time period. This finding is similar to other studies of children with cancer and SCD that show that this population may need additional weeks to complete computerized training (Hardy et al., 2016; Kesler, Lacayo, & Jo, 2011).

Greater than one third of the sample did not complete any sessions. These participants all had a diagnosis of SCD and likely experience more barriers to adherence than children with a history of a brain tumor who are off treatment (i.e. pain, fatigue). In addition, both partial completers and non-completers reported themselves at the lower-end of annual income. These participants may experience more barriers to participation as well (i.e., problems with internet access). In fact, reasons cited for not participating in the program included lack of internet access and an increase in parent's work hours, which likely lead to a decrease in parent monitoring of the program. Participants also cited health problems and a death in the family as reasons for not participating.

Overall, parents rated the program as feasible, noting that they were happy with the results of Cogmed and would recommend Cogmed to others. Thus, Hypothesis 1b related to the consumer ratings of feasibility was generally supported. In addition, most parents reported that training over the summer was convenient. Interestingly, less than half of parents reported that training over the summer allowed more flexibility. The findings may suggest that while training over the summer is convenient for some families, this time period may not be conducive to training for all families. Future studies may consider getting feedback from families as to what time of year works best for them or provide additional supports for summer training (i.e. daily reminder texts).

Hypothesis 2, that there would be a significant difference between groups on measures of working memory was not supported. This is likely due to the small sample size. Follow up analyses indicated a large effect size for improvements in group means for completers on the working memory composite, letter-number sequencing, and digit span tests versus a small effect size for non-completers on the working memory composite and both working memory subscales. These findings are similar to results obtained by Hardy and colleagues, who demonstrated large effect sizes immediately following the intervention as well as at the 3-month follow up, at which time results were no longer significant (2013). Partial completers also demonstrated medium to large effect sizes on measures of working memory, although not as large as completers. It is possible that engaging in a reduced number of training sessions may lead to a benefit for some children. Future studies could consider examining the least amount of sessions that would lead to improvement in this population using a larger sample to better establish the reliability of the effect sizes observed in the present study. Interestingly, picture span showed a small effect size for all three groups. This is a relatively new test of visuospatial working memory. Its sensitivity to change over time and other psychometric properties are less well understood than the other WISC-V measures.

The hypothesis that gains in working memory would generalize to measures of functional attention and working memory was not supported. All three groups tended to improve on subtests of the TEA-Ch, perhaps due to practice effects, with no statistically significant improvements related to completing CogMed. Interestingly, non-completers performed more poorly on the TEA-Ch across subscales at baseline. This finding suggests that the TEA-Ch may capture an aspect of attention and executive function that isn't measured on the WISC-V, but could be an important moderator of a child's ability to engage in the training. Specifically, the TEA-Ch may provide additional information on a child's ability to sustain attention, switch between two tasks, and inhibit a response; abilities necessary to complete a computerized working memory program. The TEA-Ch may also tap into an individual's capacity for directed attention, which refers to the ability to pay attention to stimuli that aren't particularly interesting (Kaplan & Berman, 2010). Children who are low on this resource may be less likely to complete a cognitive training program. While other studies have measured attention at baseline, this is the first study to measure differences in attention in eligible children that have failed to complete study procedures and may indicate a factor that presents an additional barrier to completing the program.

Despite several important findings gained from this study, some methodological issues limit study generalizability. The small sample size, although comparable to other cognitive training studies conducted with this population, warrants caution when interpreting effect sizes. A study with a larger sample size could help to determine the optimal time of year for working memory training and be more conducive to additional adaptations that families could access in order to improve adherence. In addition, lack of a comparison group limits interpretation of results to conclude that training during the summer does not reduce barriers in this population. It is possible that participation would have been even lower (or higher) if completed during the school year. Finally, there were unequal numbers of participants with history of brain tumor versus SCD in the sample. Although both groups were recruited with similar procedures, children with SCD with working memory problems were more prevalent in the clinic sample in comparison to children with cancer. Future studies should examine whether a similar protocol is effective for both children with cancer and SCD or whether specific adaptations should be tailored to each illness group.

REFERENCES

Alloway, T.P. & Alloway, R.G. (2010). Investigating the predictive roles of working memory and IQ in academic attainment. *Journal of Experimental Child Psychology*, 106, 20-29.

American Academy of Pediatrics Medical Home Initiatives for Children with Special Needs Project Advisory Committee (2002). The medical home. *Pediatrics*, *110*(1), 184-186.

Armstrong, D. F., Pavlakis, S., Goldman, M.L., Thompson, W., Cuadra, A.,& Sulc, W. (2010).Neurocognitive outcomes in sickle cell disease. In R. Nass&Y. Frank (Eds.), Cognitive and behavioral abnormalities of pediatric diseases. New York: Oxford University Press.

Armstrong, F.D., Thompson, R.J., Wang, W., Zimmerman, R., Pegelow, C.H.,…, & Vass, K. (1996). Cognitive functioning and brain magnetic resonance imaging in children with sickle cell disease. Pediatrics, 97(6), 864-870.

Ashford, J., Schoffstall, C., Reddick, W.E., Leone, C., Laningham, F.H.,…, & Conklin, H.M. (2010). Attention and working memory abilities in children treated for acute lymphoblastic leukemia. Cancer, *116*, 4638-4645.

Baddeley, A. (1992). Working memory. *Science*, 255(5044), 556-559.

Baddeley, A. (2003). Working memory: Looking back and looking forward. *Nature Reviews Neuroscience*, *4*, 829-839.

Beck, S.J., Hanson, C.A., Puffenberger, S.S., Benninger, K.L., Benninger, W.B. (2010). A controlled trial of working memory training for children and adolescents with ADHD. *Journal of Clinical Child and Adolescent Psychology*, *39*(6), 825-836.

Bertisch, H., Rath, J.F., Langenbahn, D.M., Sherr, R.L., & Diller, L. (2011). Group treatment in acquired brain injury rehabilitation. *The Journal for Specialists in Group Work*, *36*(4), 264-277.

Bracy, O.L., Oakes, A.L., Cooper, R.S., Watkins, D., Watkins, M.,…, & Jewell, C. (1999). The effects of cognitive rehabilitation therapy techniques for enhancing the cognitive/intellectual functioning of seventh and eighth grade children. *Cognitive Technology*, *4*(1), 19-27.

Brandling-Bennett, E.M. (2003). Patterns of verbal and long-term working memory performance reveal deficits in strategic processing in children with frontal infarcts related to sickle cell disease. *Developmental Neuropsychology*, *24*(1), 423-434.

Brown, R.T., Madan-Swain, A., Pais, R., Lambert, R.G., Sexson, S., & Ragab, A. (1992). Chemotherapy for acute lymphoblastic leukemia: Cognitive and academic sequelae. *The Journal of Pediatrics*, *121*(6), 885-889.

Brown, R.T., Madan-Swain, A., Walco, G.A., Cherrick, I., Ievers, C.E.,…, & Lauer, S.J. (1998). Cognitive and academic late effects among children previously treated for acute lymphoblastic leukemia receiving chemotherapy as CNS phophylaxis. *Journal of Pediatric Psychology*, *23*(5), 333-340.

Butler, R.W. & Copeland, D.R. (2002). Attentional processes and their remediation in children treated for cancer: A literature review and the development of a therapeutic approach. *Journal of the International Neuropsychological Society*, *8*, 115-124.

Butler, R.W., Copeland, D.R., Fairclough, D.L., Mulhern, R.K., Katz, E.R.,…, & 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.

Butler, R.W. & Mulhern, R.K. (2005). Neurocognitive interventions for children and adolescents surviving cancer. *Journal of Pediatric Psychology*, *30*(1), 65-78.

Cappa, S.F., Benke, T., Clarke, S., Rossi, B., Stemmer, B., & Van Heugten, C.M. (2005). EFNS guidelines on cognitive rehabilitation: Report of an EFNS task force. *European Journal of Neurology*, *12*, 665-680.

Carey, M.E., Hockenberry, M.J., Moore, I.M., Hutter, J.J., Krull, K.R., Pasvogel, A., & Kaemingk, K.L. (2007). Brief report: Effect of intravenous methotrexate dose and infusion rate on neuropsychological function one year after diagnosis of acute lymphoblastic leukemia. *Journal of Pediatric Psychology*, *32*(2), 189-193.

Chacko, A., Bedard, A.C., Marks, D.J., Feirsen, N., Uderman, J.Z.,…, & Ramon, M. (2014). A randomized clinical trial of Cogmed working memory training in school-age children with ADHD: A replication in a diverse sample using a control condition. *The Journal of Child Psychology and Psychiatry, 55*(3), 247-255.

Cicerone, K.D., Dahlberg, C., Kalmar, K., Langhenbahn, D.M., Malec, J.F.,…, & Kneipp, S. (2000). Evidenced-based cognitive rehabilitation: Recommendations for clinical practice. *Archives of Physical Medicine Rehabilitation*, *81*, 1596-1615.

Cockcroft, K. (2011). Working memory functioning in children with attention deficit/hyperactivity disorder (ADHD): A comparison between subtypes and normal controls. *Journal of Child and Adolescent Mental Health*, *23*(2), 107-118.

Conklin, H.M., Ashford, J.M., Howarth, R.A., Merchant, T.E., Ogg, R.J.,…, & Xiong, X. (2012). Working memory performance among childhood brain tumor survivors. *Journal of the International Neuropsychology Society*, *18*(6), 996-1005.

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.

Copeland, D.R., Dowell, R.E., Fletcher, J.M., Bordeaux, J.D., Sullivan, M.P.,…, & Cangir, A. (1988). Neuropsychological effects of childhood cancer treatment. *Journal of Child Neurology*, *3*, 53-62.

Copeland, D.R., deMoor, C., Moore, B.D., & Ater, J.L. (1999). Neurocognitive development of children after a cerebellar tumor in infancy: A longitudinal study. *Journal of Clinical Oncology*, *17*(1), 3476-3486.

Cox, L.E., Ashford, J.M., Clark, K.N., Martin-Elbahesh, K., Hardy, K.K.,…, & 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.

Daly, B., Kral, M.C., & Tarazi, R.A. (2011). The role of neuropsychological evaluation in pediatric sickle cell disease. *The Clinical Neuropsychologist*, *25*(6), 903–925.

Daneman, M. & Carpenter, P.A. (1983). Individual differences in integrating information between and within sentences. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *9*(4), 561-584.

DeBaun, M.R., King, A.A., & White, D.A. (2008). Need for cognitive rehabilitation for children with sickle cell disease and strokes. *Expert Review of Neurotherapeutics*, *8*(2), 291-296.

Dehn, M.J. (2008). *Working memory and academic learning assessment*. Hoboken, NJ: John Wiley & Sons, Inc.

Dennis, M., Hetherington, C.R., & Speigler, B.J. (1998). Memory and attention after childhood train tumors. *Medical and Pediatric Oncology Supplement*, *1*, 25-33.

Dowell, R.E., Copeland, D.R., Fletcher, J.M., & Stovall, M. (1991). Absence of synergistic effects of CNS treatments on neuropsychologic test performance among children. *Journal of Clinical Oncology*, 9, 1029-1036.

Duchnowski, A.J. & Kutash, K. (2011). School reform and mental health services for Students with emotional disturbances educated in urban schools. *Education and Treatment of Children*, *34*(3), 323-346.

Dunning, D.L., Holmes, J., & Gathercole, S.E. (2013). Does working memory training lead to generalized improvements in children with low working memory? A randomized controlled trial. *Developmental Science*, *16*(6), 915-925.

Egeland, J., Aarlien, A.K., & Saunes, B. (2013). Few effects of far transfer of working memory training in ADHD: A randomized controlled trial. *PLoS ONE*, *8*(10).

Fry, A.F. & Hale, S. (1996). Processing speed, working memory, and fluid intelligence. *Psychological Science*, *7*(4), 237-241.

Fry, A.F. & Hale, S. (2000). Relationships among processing speed, working memory, and fluid intelligence in children. *Biological Psychology*, *54*, 1-34.

Gathercole, S.E. & Pickering, S.J. (2000). Working memory deficits in children with low achievements in the national curriculum at 7 years of age. *British Journal of Educational Psychology*, *7*, 177-194.

Geenen, M.M., Cardous-Ubbink, M.C., Kremer, L.C.M., van den Bos, C., van der Pal, H.J.H.,…, & van Leeuwen, F.E. (2007). Medical assessment of adverse health outcomes in long-term survivors of Childhood cancer. *Journal of the American Medical Association*, *297*(24), 2705-2715.

Gehring, K., Aaronson, N.K., Taphoorn, M.J.B., & Sitskoorn, M.M. (2011). A description of a cognitive rehabilitation programme evaluated in brain tumour patients with mild to moderate cognitive deficits. *Clinical Rehabilitation*, *25*(8), 675-692.

Hardy, K.K., Willard, V.W., & Bonner, M.J. (2011). Computerized cognitive training in survivors of childhood cancer: A pilot study. *Journal of Pediatric Hematology/Oncology Nursing*, *28*(1), 27-33.

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*, 1856-1865.

Hardy, S.J., Hardy, K.K., Schatz, J.C., Thompson, A.L., & Meier, E.R. (2016). Feasibility of home-based computerized working memory training with children and adolescents with sickle cell disease. *Pediatric Blood & Cancer*, *63*(9), 1578 1585.

Herzer, M., Godiwala, N., Hommel, K., Driscoll, K., Mitchell, M.,…, & Modi, A.C. (2010). Family functioning in the context of pediatric chronic conditions. *Journal of Developmental & Behavioral Pediatrics*, *31*(1), 26-34.

Jaeggi, S.M., Buschkuehl, M., Shah, P., & Jonides, J. (2013). The role of individual Differences in cognitive training and transfer. *Memory and Cognition*, *42*, 464-480.

Kesler, S.R., Lacayo, N.J., & Jo, B. (2011). A pilot study of an online cognitive rehabilitation program for executive function skills in children with cancer-related brain injury. *Brain Injury*, *25*(1), 101-112.

King, T.Z., Fennell, E.B., Williams, L., Algina, J., Boggs, S.,…, & Leonard, C. (2004). Verbal memory abilities of children with brain tumors. *Child Neuropsychology*, *10*(2), 76-88.

King, A.A., White, D.A., McKinstry, R.C., Noetzel, M., & DeBaun, M.R. (2007). A pilot randomized education rehabilitation trial is feasible in sickle cell and strokes. *Neurology*, *68*, 2008-2011.

Klingberg, T., Fernell, E., Olesen, P.J., Johnson, M., Gustaffson, P.,…, & Westerberg, H. (2005). Computerized training of working memory in children with ADHD: A randomized controlled trial. *American Academy of Child & Adolescent Psychiatry*, *44*(2), 177-186.

Klingberg, T., Forssberg, H., & Westerberg, H. (2002). Training of working memory in children with ADHD. *Journal of Clinical and Experimental Neuropsychology*, *24*(6), 781-791.

Kronenberger, W.G., Pisoni, D.B., Henning, S.C., Colson, B.G., & Hazzard, L.M. (2011). Working memory training for children with cochlear implants: A pilot study. *Journal of Speech, Language, and Hearing Research*, *54*, 1182-1196.

Lee, Y., Nauert, C., & Glass, J.P. (1986). Treatment-related white matter changes in cancer patients. Cancer, 57, 1473-1482.

Mackey, A.P., Hill, S.S., Stone, S.I., & Bunge, S.A. (2011). Differential effects of reasoning and speed training in children. *Developmental Science*, *14*(3), 582-590.

Manly, T., Anderson, V., Nimmo-Smith, I., Turner, A., Watson, P., & Robertson, I.H. (2001). The differential assessment of children's attention: The test of everyday attention for children (TEA-Ch), normative sample and ADHD performance. *Journal of Child Psychology and Psychiatry*, *42*(8), 1065-1081.

Manly, T., Robertson, I.H., Anderson, V., & Nimmo-Smith, I. (1999). *TEA-Ch: The test* *of everday attention for children manual*. Bury St. Edmunds, UK: Thames Valley Test Company.

McCabe, D.P., Roediger, H.L., McDaniel, M.A., Balota, D.A., & Hambrick. D.Z. (2010). The relationship between working memory capacity and executive functioning: Evidence for a common executive attention construct. *Neuropsychology*, *24*(2), 222-243.

Melby-Lervag, M. & Hulme, C. (2013). Is working memory training effective? A meta analytic review. *Developmental Psychology*, *49*(2), 270-291.

Mitchell, M.J., Lemanek, K., Palermo, T.M., Crosby, L.E., Nichols, A., & Powers, S.W. (2007). Parent perspectives on pain management, coping, and family functioning in pediatric sickle cell disease. *Clinical Pediatrics*, *46*(4), 311-319.

Mitchell, C. & Begeny, J.C. (2014). Improving student reading through parents implementation of a structured reading program. *School Psychology Review*, *43*(1) 41-58.

Moleski, M. (2000). Neuropsychological, neuroanatomical, and neurophysiological consequences of CNS chemotherapy for acute lymphoblastic leukemia. *Archives of Clinical Neuropsychology*, *15*(7), 603-630.

Moore, B.D. (2005). Neurocognitive outcomes in survivors of childhood cancer. *Journal of Pediatric Psychology*, *30*(1), 51-63.

Moore, B.D., Copeland, D.R., Ried, H., & Levy, B. (1992). Neurophysiological basis of cognitive deficits in long-term survivors of childhood cancer. *Archives of Neurology*, *49*, 809-817.

Mulhern, R.K., White, H.A., Glass, J.O., Kun, L.E., Leigh, L.,…, & Reddick, W.E. (2004). Attentional functioning and white matter integrity among survivors of malignant brain tumors of childhood. *Journal of the International Neuropsychological Society*, *10*, 180-189.

Patel, S.K., Katz, E.R., Richardson, R., Rimmer, M., & Killian, S. (2009). Cognitive and problem solving training in children with cancer: A pilot project. The *American Journal of Pediatric Hematology/Oncology*, *31*(9), 670-677.

Pini, S., Hugh-Jones, S., & Gardner, P.H. (2012). What effect does a cancer diagnosis have on educational engagement and school life of teenagers? *Psycho-Oncology*, *21*, 685-694.

Puddy, R.W., Roberts, M.C., Verberg, E.M., & Hambrick, E.P. (2012). Service coordination and children's functioning in a school-based intensive mental health program. *Journal of Child and Family Studies*, *21*, 948-962.

Rajender, G., Malhotra, S., Bhatia, M.S., Singh, T.B., & Kanwal, K. (2011). Efficacy of cognitive retraining techniques in children with attention deficit hyperactivity disorder. *German Journal of Psychiatry*, *14*(2), 55-59.

Reimers, T.S., Ehrenfels, S., Mortensen, E.L., Schmiegelow, M., Sonderkaer, S.,…, & Muller, J. (2003). Cognitive deficits in long-term survivors of childhood brain tumors: Identification of predictive factors. *Medical and Pediatric Oncology*, *40*, 26-34.

Schatz, J. (2004). Brief report: Academic attainment in children with sickle cell disease. *Journal of Pediatric Psychology*, *29*(8), 627-633.

Schatz, J., Brown, R.T., Pascual, J.M., Hsu, L., & DeBaun, M.R. (2001). Poor school and cognitive functioning with silent cerebral infarcts and sickle cell disease. *Neurology*, *56*, 1109-1111.

Schatz, J. & Roberts, C.W. (2005). Short-term memory in children with sickle cell disease: Executive versus modality-specific processing deficits. *Archives of Clinical Neuropsychology*, *20*, 1073-1085.

Schuurs, A. & Green, H.J. (2013). A feasibility study of group cognitive rehabilitation for cancer survivors: Enhancing cognitive function and quality of life. *Psycho-Oncology*, *22*, 1043-1049.

Shah, P, Buschkuehl, M., Jaeggi, S., & Jonides, J. (2012). Cognitive training for ADHD: The importance of individual differences. *Journal of Applied Research in Memory and Cognition*, *1*, 204-205.

Sherr, R.L. & Langenbahn, D.M. (1992). An approach to large-scale outpatient neuropsychological rehabilitation. *Neuropsychology*, *6*(4). 417-426.

St. Clair Thompson, H., Stevens, R., Hunt, A., & Bolder, E. (2010). Improving children's working memory and classroom performance. *Educational Psychology*, *30*(2), 203-219.

Takeuchi, H., Sekiguchi, A., Taki, Y., Yokoyama, S., Yomogida, Y.,…, & Kawashima, R. (2010). Training of working memory improves structural connectivity. *The Journal of Neuroscience*, *30*(9), 3297-3303.

Turner, C.D., Rey-Casserly, C., Liptak, C.C., & Chordas, C. (2009). Late effects of therapy for pediatric brain tumor survivors. *Journal of Child Neurology*, 24(11), 1455-1463.

Van't Hooft, I. & Norberg, A.L. (2010). SMART cognitive training combined with a parental coaching programme for three children treated for medulloblastoma. *Neurorehabilitation*, *26*, 105-113.

Varni, J.W., Katz, E.R., Colegrove, R., & Dolgin, M. (1996). Family functioning predictors of adjustment in children with newly diagnosed cancer: A prospective analysis. *Journal of Child Psychology and Psychiatry*, *37*(3), 321-328.

Wallander, J.L., Varni, J.W., Babani, L., Banis, H.T., & Wilcox, K.T. (1989). Family resources as resistance factors for psychological maladjustment in chronically ill and handicapped children. *Journal of Pediatric Psychology*, *14*(2), 157-173.

Ward, E., DeSantis, C., Robbins, A., Kohler, B., & Jemal, A. (2014). Childhood and adolescent cancer statistics. *CA: A Cancer Journal for Clinicians*, *64*, 83-103.

White, D.A., Salorio, C.F.,Schatz, J., & Debaun, M. (2000). Preliminary study of working memory in children with stroke related to sickle cell disease. *Journal of Clinical and Experimental Neuropsychology*, *22*(2), 257-264.

Wechsler, D. (2014). *Wechsler intelligence scale for children, fifth edition manual*. Bloomington, MN: Pearson.

Yerys, B.E., White, D.A., Salorio, C.F., McKinstry, R., Moinuddin, A., & DeBaun, M. (2003). Memory strategy training in children with cerebral infarcts related to sickle cell disease. *Journal of Pediatric Hematology/Oncology*, *25*(6), 495-498.