Cognitive Functioning, Coping, and Emotional Distress in Children with Sickle Cell Disease

By

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ABSTRACT

Sickle cell disease is a chronic lifelong illness that affects 1 in 400 to 500 African Americans in the United States. In addition to being at increased risk for cognitive deficits, children with sickle cell disease may also be at greater risk for emotional distress. The current study investigates the relationship between cognitive functioning, coping, and emotional distress in children and adolescents with SCD. Forty-seven children with sickle cell disease completed cognitive assessments assessing working memory and verbal comprehension, and their parents completed questionnaires that reported on child coping and emotional distress. Results showed that verbal comprehension was significantly associated with secondary control coping. Both working memory and secondary control coping were associated with depressive symptoms. Further analyses showed that verbal comprehension had an indirect association with depressive symptoms through secondary control coping, whereas working memory only had a direct association with depressive symptoms. The implication of these findings are discussed.

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CHAPTER I

INTRODUCTION

Sickle cell disease (SCD) is a genetic hemoglobin disorder that occurs in approximately 1 in 400 to 500 African Americans in the United States (Hassell, 2010). SCD presents three specific challenges to children's development. First, the disease poses significant sources of stress related to recurrent pain, disruptions in daily role functioning, and uncertainty about the illness and the future (Hildenbrand, Barakat, Alderfer, & Marsac, 2013; Prussien et al., 2016). Second, SCD places children at risk for significant cognitive impairments (Schatz, Finke, Kellett, & Kramer, 2002; Yarboi et al., 2015). Third, the way children are able to cope with the stressors related to the disease is important for psychosocial distress (Compas, Jaser, Dunn, & Rodriguez, 2012), and their ability to cope may be influenced by their cognitive functioning (Campbell et al., 2009). The goal of the present research is to assess how children and adolescents with SCD cope with the stress of the illness, how their coping is related to emotional distress, and to determine the direct and indirect associations between cognitive functioning and distress through coping strategies.

Sickle Cell Disease: An Overview

SCD describes the group of hemoglobin disorders in which there is either a homogenous pair of the sickle hemoglobin (HbS) or a heterogeneous pair of HbS and a different abnormal hemoglobin gene. The most common subtype, HbSS, also known as sickle cell anemia, occurs in 65% of those with the disease, followed by HbSC (25%), $HbS\beta^{+}$thalaseemia (8%), and $HbS\beta^{0}$thalaseemia (2%; Platt et al., 2001), with HbSS and $HbS\beta^{0}$thalaseemia having more severe biological characteristics. The presence of HbS causes red blood cells to form a long sickle shape and inhibits these cells from properly transporting oxygen throughout the body. SCD commonly results in medical difficulties including chronic anemia, recurrent pain crises, splenic sequestration, and even stroke. Although the medical complications of the disease are associated with shortened lifespan (Platt et al., 1994), recent treatments such as hydroxyurea, a chemotherapy drug used to increase levels of fetal hemoglobin and prevent the red blood cells from sickling, and chronic transfusions, used to decrease the percentage of HbS in the blood stream, have been shown to improve medical symptoms, increase quality of life, and reduce rates of mortality in individuals with SCD (Stegenga, Ward-Smith, Hinds, Routhieaux, & Woods, 2004; Steinberg et al., 2003; Thornburg, Calatroni, & Panepinto, 2011).

Cognitive Deficits in Pediatric SCD

As a function of disease and environmental factors, children with SCD are at an increased risk for deficits in cognitive functioning compared to their typically developing peers (e.g., Schatz et al., 2002; Steen et al., 2005; Yarboi et al., 2015). In a comprehensive meta-analysis, Schatz and colleagues (2002) analyzed 14 previously published studies that assessed intelligence in children and adolescents with SCD without a history of cerebral infarction. They found that the average Full Scale IQ (FSIQ) of children with SCD was 86.4, which was 4.3 standard score points lower (d = -0.31) than that of healthy controls and 13.6 IQ points lower than national norms. Schatz et al. also showed that this effect was even more pronounced when assessing specific areas of cognitive functioning. Seventy-one percent of the investigated studies found that children with SCD were significantly impaired in domains of attention, executive functioning, memory, and language. Further, these deficits were associated with age, such that the difference in cognitive functioning between children with SCD and the normative population increased with age.

As mentioned above, executive functioning (EF) in particular has been shown to be significantly lower in children with SCD compared to healthy peers (Schatz, Brown, Pascual, Hsu, & DeBaun, 2001). One theory proposes a three-component model of EF, composed of updating, shifting, and inhibition (Friedman et al., 2008; Miyake et al., 2000). Updating involves adding relevant information to working memory while, at the same time, removing irrelevant information. Shifting is defined as switching between cognitive tasks and rules with ease. Finally, inhibition involves the ability to suppress an automatic or learned response. In addition to the three-component model, studies have also identified other aspects of EF, including planning, verbal working memory, and verbal fluency (Snyder, 2013). Multiple studies have shown that while these components are all moderately related, they are separate and distinct within the EF construct (Fisk & Sharp, 2004; Friedman et al., 2006; Goel & Grafman, 1995; Hedden & Yoon, 2006; Miyake et al., 2000). With regard to children with SCD, Yarboi et al. (2015) assessed EF using the Trial Making Task and the Color/Word Interference Task from the Delis-Kaplan Executive Function System (D-KEFS; Delis, Kaplan, & Kramer, 2001). Results of this study showed that pediatric SCD patients scored significantly lower than the normative mean on the Trial Making Task Number/Letter Switching Condition and the Color/Word Interference Inhibition Switching condition. When considering the three-component model of EF, this finding suggests that children with SCD have deficits in both shifting and inhibition.

Children with SCD also show significant deficits in verbal comprehension and reasoning. Using a sample of children with severe forms of SCD (i.e, HbSS or HbSβ^0thalaseemia), Hijmans et al. (2011) found that on average children obtained a score of 83 (*SD* = 12.1) on the Verbal IQ composite of the Wechsler Intelligence Scale for Children, Third Edition (WISC-III; Wechsler, 1991). This score was 10 IQ points below the SES-matched controls (*M* = 93, *SD* = 15.1, *d* = .7) and 17 points below the standardized mean (Hijmans et al.). Other studies have shown similar findings, with verbal comprehension scores ranging from 80.33 to 94.97 on standardized assessments (Schatz & Roberts, 2005; Steen et al., 2005; Yarboi et al., 2015).

Biological risks for cognitive impairment. Cerebral infarction (i.e., stroke) is the most-common cause of neurological damage in children with SCD (Ohene-Frempong et al., 1998). Silent strokes, ischemic cerebral infarcts that do not have the immediate and visible symptoms that are associated with overt strokes, occur in up to 30% of children with SCD under 6 years of age (Kwiatkowski et al., 2009). Despite being defined as silent, these cerebral infarcts are associated with significantly lower general intelligence and lower scores in specific areas of cognitive functioning compared to the normative mean (Watkins et al., 1998). For example, using a sample of 173 children with SCD, Bernaudin et al. (2000) found that those with a history of silent strokes were at significantly increased risk for deficits in Performance IQ and FSIQ. Further, in their meta-analysis of 10 studies, King et al. (2014) showed that although all children with SCD displayed deficits in FSIQ ($M = 86.54$), those with a history of one or more silent strokes were more severely impaired, with an overall effect of -4.76 IQ points compared to those without a history of stroke. Finally, while silent cerebral infarcts are associated with deficits in FSIQ, Armstrong et al., (1996) also found that intelligence scores were lowest in children with a history of an overt stroke.

Other medical risks associated with cognitive deficits in this population include increased cerebral blood flow (CBF) velocity, disordered breathing during sleep, and chronic anemia. While increased CBF velocity can cause disturbances in the brain that result in stroke, studies have also found that abnormal CBF in the absence of silent or overt stroke is associated with deficits in cognitive functioning (Adams et al., 1992; Sanchez, Schatz, & Roberts, 2010; Strouse et al., 2006). Related to CBF, sleep disordered breathing is also a significant predictor of cognitive deficits in this population (Hill et al., 2006). Nearly 40% of children with SCD experience sleep disordered breathing (Needleman et al., 1999), and this results in low hemoglobin oxygenation that negatively affects general intelligence and specific domains of EF (Hollocks et al., 2012). Finally, even basic disease characteristics, such chronic anemia, have also been found to be significantly associated with Verbal IQ, Performance IQ, and FSIQ (Bernaudin et al., 2000; Hijmans et al., 2011; Steen et al., 2003). Steen et al. (2003) found that the degree of chronic anemia explained 23% of the variance in predicting FSIQ in children with SCD without a history of stroke. Similar to conclusions about sleep-disordered breathing, researchers have hypothesized that the relationship between chronic anemia with deficits in cognitive functioning may be due to massive deoxygenation of the brain (Steen et al.).

Environmental risks for cognitive impairment. Outside of these medical risks, environmental factors are also significantly associated with intelligence and EF in children with SCD. In addition to the biomedical sequelae of the disease, children with SCD often grow up in low socioeconomic status (SES) households. For example, King et al. (2014) found that characteristics of the home environment and parental education were significant predictors of FSIQ within this population. Children living with a parent who had some college education scored 6.2 IQ points higher than children living with a parent who had no college education (King et al.). This finding remained significant even when controlling for history of silent cerebral infarct. Results for household income showed that each additional $1000 per capita was associated with a 0.33-point increase in FSIQ (King et al.). Further, Yarboi et al. (2015) found that mothers' report of social-environmental stress is also associated with levels of cognitive function in children with SCD. Increased maternal financial stress was the strongest predictor of deficits across all domains of cognitive functioning and academic achievement scores (i.e., Verbal IQ, Performance IQ, FSIQ, academic achievement, and measures of executive functioning; Yarboi et al.).

Executive Functioning and Distress

Cognitive function, including aspects of EF, is related to emotional distress, the ability to regulate emotions, and the ability to cope with stress. Therefore, impairments in cognitive function can have wide effects on children's behavioral and social development. Specific deficits associated with increased risk for emotional problems include difficulty initiating cognitive strategies (Hertel & Gerstle, 2003), slowed processing speed (Hartog, Derix, Van Bemmel, Kremer, & Jolles, 2003), and overall depleted cognitive resources (Matthews & MacLeod, 1994).

EF has been shown to be most-consistently associated with anxiety and major depressive disorder (MDD; Moran, 2016; Snyder, 2013). A meta-analysis assessing 177 samples showed that self-reports of anxiety symptoms were significant associated with deficits in working memory (Moran, 2016). A separate meta-analysis conducted by Snyder (2013) assessed the association between multiple components of EF and MDD across 113 studies. There was a reliable association between EF and MDD such that participants with lower scores on EF measures had more severe symptoms of depression, with effect sizes ranging from $d = 0.32$ to 0.97. Patients with MDD also demonstrated lower scores on processing speed ($d = 0.33$), impairments in inhibition ($d = 0.58$), shifting ($d = 0.47$), updating ($d = 0.57$), verbal working memory ($d = 0.45$), and a small effect for verbal fluency ($d = 0.14$). It must be noted, however, that the direction of the association between EF and depression is still unknown. That is, EF is theorized to be a causal link for a variety of different psychopathologies (Fioravanti, Carlone, Vitale, Cinti, & Clare, 2005; Olley, Malhi, & Sachdev, 2007; Willcutt, Doyle, Nigg, Faraone, & Pennington, 2005), but EF and psychopathology may both be a result of neurobiological differences or structural differences in the brain caused by stress (Holmes & Wellman, 2009; Nugent, Tyrka, Carpenter, & Price, 2011; Tsunoka et al., 2009). The relationship between working memory and anxiety, however, appears to move in a direction such that anxiety precedes deficits in working memory, and it impedes performance on assessments and measures of functioning (Moran, 2016). While there is also ample evidence for the association between EF and externalizing problems, internalizing problems will be the primary focus for this project.

Stress and Distress in Pediatric SCD

Distress is also related to experiences of acute and chronic stressors experienced within the environment. Chronic illness is a significant source of stress for children and adolescents, and in addition to this their lives are influenced by other normative developmental stressors as well. Further, much of the disease-related stress children with serious illnesses encounter is outside of their personal control (Compas et al., 2012). For example, children with SCD have limited or no control over pain crises, how many days of school they miss due to hospital visits, or their level of physical exhaustion when playing with friends. Hildenbrand et al. (2015) used a mixed methods design to assess the different stressors related to SCD for children and their caregivers. After conducting multi-informant semi-structured interviews evaluating different sources of stress, the authors categorized the responses into seven categories: medical complications (i.e., pain, bedwetting), treatment and side effects (i.e., taking medications, hospital visits/stays), disruption in daily routines and activities (i.e., missing school, being unable to participate in activities), emotional reactions, communication issues (i.e., speaking with doctors, telling friends about SCD), social challenges (i.e., feeling or looking different from others), and concerns about the future (i.e., transition to adulthood, adult health). Although many previous studies investigating stress in pediatric SCD have focused primarily on pain crises (e.g., Gil, Williams, Thompson, & Kinney, 1991; Mitchell et al., 2007; Schlenz, Schatz, McClellan, Sweitzer, & Roberts, 2013), it is clear that children with SCD are affected by various stressors that include, but are not limited to, pain.

Stress in pediatric SCD samples can also influence disease-related symptoms and health management outcomes. For example, Gil et al. (2003) found that increases in daily stress were associated with an increase in same-day pain and negative mood in adolescents with SCD. Because pain is a significant source of stress in addition to being an outcome, the researchers also tested a reverse path between the two variables. They found that pain was also a significant predictor of subsequent increase in stress levels two days later. Gil et al. also showed that increases in daily stress were associated with an increase in healthcare use, school absences, and a reduction in social activity even when controlling for pain. While this study was the only one of its kind to demonstrate the relationship between stress and pain in children with SCD, other studies have also shown this relationship in adults with SCD (Porter et al., 1998) and other pediatric populations (e.g., Walker, Garber, Smith, Van Slyke, & Claar, 2001).

Children who experience high rates of disease-related stress are also at greater risk for experiencing symptoms of depression and anxiety (Compas et al., 2012; Rodriguez et al., 2012); however, there have been inconsistent findings in whether or not children and adolescents with SCD experience increased rates of emotional distress. Some studies show that children and adolescents with SCD are at a higher risk for experiencing symptoms of distress. For example, Thompson et al. (1998) reported that children and adolescents with SCD experience more internalizing symptoms than their peers. Using the Children's Depression Inventory (CDI;

Kovaks, 1981), Morgan and Jackson (1986) also found that adolescents with SCD had more symptoms of depression and greater social withdrawal than controls. Finally, Trzepacz et al. (2004) used the CBCL to assess emotional distress in this population, and they showed that children with SCD experienced more internalizing symptoms compared to age-matched peers and were also significantly more likely to exceed clinical cutoffs.

While it appears that children and adolescents with SCD are at an increased risk for experiencing symptoms of depression and anxiety, other studies have concluded the exact opposite (Benton, Ifeagwu, & Smith-Whitley, 2007). Despite finding that 29% of adolescents with SCD had high symptoms of depression, whereas only 12% of the healthy controls obtained high scores on the Children's Depression Rating Scale – Revised (Poznanski, Freeman, & Mokros, 1985; Yang, Cepeda, Price, Shah, & Mankad, 1994), Yang et al. concluded that the scores obtained by the adolescents with SCD were inflated by somatic symptoms of the disease (e.g., fatigue) and that the reported difference was not qualitatively significant. Kumar, Powars, Allen, and Haywood (1976) reported that on average their sample of 29 adolescents with HbSS was less anxious compared to their peers, yet they were still more likely to display withdrawn behaviors and hold a poorer self-concept. Finally, Lemanek, Moore, Gresham, Williamson, and Kelley (1986) concluded that children with SCD did not differ significantly from age, gender, SES, and IQ-matched controls in their levels of psychological maladjustment.

The contradictory findings regarding whether or not children with SCD experience increased symptoms of emotional distress could be explained by the use of measures that use somewhat arbitrary cutoff points to imply diagnoses in children and adolescents. Dichotomizing a sample into a case versus a non-case is not the ideal view of psychopathology; anxiety and depression are better studied dimensionally rather than categorically (e.g., Hudziak, Achenbach, Althoff, & Pine, 2007). Further, studies concluding that children with SCD do not experience internalizing symptoms only emphasize differences compared to controls and do not focus any attention on the deviation from the nationally standardized mean. For example, although Lemanek et al. (1986) concluded that children with SCD do not demonstrate significantly greater psychological maladjustment, they also reported that the average *T*-score (a standardized score with a mean of 50 and a standard deviation of 10) within the SCD children for internalizing problems was 59.21, nearly a full standard deviation above the standardized mean. The case could also be made that when the control sample within a study also demonstrates elevated symptoms of distress relative to the standardized norm, this control sample may not be representative. Nevertheless, while some studies show that children with SCD may not be at an increased risk for emotional distress compared to their peers, it is clear that they do experience elevated symptoms of depression and anxiety.

Coping with Pediatric SCD

While stress has a direct effect on the experience of pain, health behaviors, and internalizing problem in children with SCD, it is not the only factor that matters. How people cope with a stressor is often more important than the experience of the stressor itself. Many of the previous studies on coping in children with SCD used Karen Gil's (1991) model of coping to assess how children with SCD cope with pain in particular using the Coping Strategies Questionnaire for SCD (Gil et al., 1991).

This model is composed of three components. The first component, termed Coping Attempts, describes children's attempts to cope with pain in cognitively and behaviorally active manner. Coping Attempts is comprised of five behaviors: diverting attention, reinterpreting pain sensations, ignoring pain sensations, calming self-statements, and increased behavior activity.

The second component, Negative Thinking, includes catastrophizing and fearful self-statements, angry self-statements, and isolation when experiencing SCD-related pain. Finally, Passive Adherence Coping includes concreate actions and behaviors that are typically recommended by healthcare professionals as methods to decrease, manage, or control pain. This component includes resting, taking fluids, praying and hoping, and applying heat, cold, or massage. Gil et al. (1991) found that children with SCD were most likely to use passive adherence when coping with the pain, followed by negative thinking, and coping attempts. While this was the original organization of the coping behaviors, later studies by the original authors and other research teams conducted additional exploratory factor analyses that highlight an inconsistent structure of the coping model (Barakat, Patterson, Tarazi, & Ely, 2007; Gil et al., 1997; Gil et al., 1993). Although the final subscales remain similar, the manifest behaviors of which they are composed change from sample to sample.

As previously noted, many studies investigating coping in pediatric SCD view pain as both a stressor and an outcome (e.g., Gil et al., 2003). Gil and Thompson (1997) assessed the efficacy pain coping using a laboratory pain task with children and adolescents with SCD. Results of a hierarchical regression analysis showed that children who used active cognitive and behavioral coping during the task had a lower tendency to report pain, even when controlling for age. Further an intervention study conducted by Schatz and colleagues (2015) showed that teaching skills within a coping intervention had a significant effect on the child's SCD-related pain, such that when adolescents used their learned coping skills on high pain days there was a significant reduction in pain intensity the next day. Also, comparing pre- and post-intervention measures, findings showed that adolescents' use of active psychological coping attempts increased over time.

Pain coping also has an impact on daily functioning outcomes in this population. Mitchell et al. (2007) found that passive coping, as opposed to negative thinking, is associated with positive family functioning and fewer emergency department visits in a sample of children and adolescents with SCD. In addition, a longitudinal descriptive study by Gil et al. (1993) showed that coping attempts were significantly associated with more involvement in school, the home, and social activities during pain crises. Passive adherence levels at baseline and increases in negative thinking from baseline to follow-up was associated with more interactions with healthcare. Gil (1993) also compared patterns of coping at baseline and 9-month follow-up. Pain coping strategies were more stable over time for younger children and more variable for adolescents. In a separate study, Gil et al. (2001) conducted a coping skills intervention with children and adolescents with SCD, and they found that children in the intervention used significantly more active coping attempts when managing pain compared to those in the control group. Results also showed that active coping attempts on days where they experienced pain was significantly associated with decreases in healthcare contacts and school absences, and increases in household activities.

In addition to its association with pain and daily functioning, the way children cope with stress is also associated with symptoms of anxiety and depression. However, research in how coping is associated with distress in children with SCD in very limited. Three studies have examined the relationship between pain coping and measures of distress. Gil et al. (1991) found that for children with SCD high levels of negative thinking and passive adherence during pain crises was associated with greater psychological distress when experiencing pain. In a separate study, Thompson, Gil, and Burbach (1993) also showed that children who primarily use negative thinking to cope with SCD-related pain had significantly higher levels of internalizing symptoms, even when controlling for disease severity such pain frequency. A more recent study showed that negative thinking was related to both depression and anxiety in pediatric SCD, and it also mediated the relationship between pain intensity and depressive symptoms (Barakat et al., 2007). In summary, studies have not found an association between active coping attempts and distress, but negative thinking has been positively associated with anxiety and depression. Further, findings on the association of passive coping with daily role functioning and distress have been inconsistent.

Control-Based Model of Coping

Much of the existing literature used the Gil's (1991) CSQ model of coping. However, recent research has provided support for a control-based model of coping in children with chronic illnesses and health conditions (Compas et al., 2012). The model is based on the theory that the actual and perceived controllability of a stressor is important in in understanding the adaptive skills that children and adolescents need to use in order to cope with it (Compas et al., 2012). In this case, chronic illness and pediatric SCD in particular presents a wide range of uncontrollable stress, as described above. The control-based model of coping organizes coping into three distinct groups: primary control coping, secondary control coping, and disengagement (Compas, Connor-Smith, Saltzman, Thomsen, & Wadsworth, 2001; Connor-Smith, Compas, Wadsworth, Thomsen, & Saltzman, 2000). Primary control coping describes behaviors and cognitive strategies that act directly to change the stressor (i.e., problem-solving) or the emotional response to the stressor (e.g., emotional expression and emotional modulation). Secondary control coping is adapting to the stressor, and this sub-factor includes cognitive reappraisal, positive thinking, and acceptance. Finally, disengagement describes a direct attempt to orient oneself away from the stressor (e.g., avoidance, wishful thinking, denial). Confirmatory factor analyses across multiple studies have shown that this three-factor model of coping is consistent in culturally diverse samples of children and adolescents coping with various types of stress (e.g., Benson et al., 2011; Compas et al., 2006; Connor-Smith & Calvete, 2004; Wadsworth, Rieckmann, Benson, & Compas, 2004; Yao et al., 2010). Compas et al. (2006) showed that the factor structure was confirmed in a sample of children coping with recurrent abdominal pain, and this finding was consistent across both parent and child reports in a latent variable analysis.

Within pediatric illnesses, the majority of the stressors experienced are highly uncontrollable; however, there are circumstances where uncontrollable situations have controllable components. Therefore, secondary control coping, for uncontrollable stressors, and primary control coping, for controllable stressors are hypothesized to be the most adaptive when it comes to reducing the risk of emotional distress. Consistent with this hypothesis, Compas et al. (2014) found that in a pediatric cancer sample, multi-informant measures of the use of primary control coping and secondary control coping with negatively associated with symptoms of anxiety and depression. Disengagement, however, was positively associated with anxiety and depression. This research group has also shown this association between coping and distress in other child and adolescent samples coping with stress of chronic pain (Compas et al. 2006), maternal depression (Compas et al., 2010), and even post-war stress (Benson et al., 2011).

Although the control-based model of coping has yet to be used with a pediatric sickle cell population, findings from a previous study using the Pediatric Pain Questionnaire (Reid et al., 1998) suggest similar outcomes when looking at individual coping behaviors. Using a sample with adolescents with SCD, Graves and Jacob (2014) showed that participants coped with pain by problem-solving, seeking information, seeking social support, and positive self-statements.

They also found that in male participants, severe pain was negatively associated with behavioral distraction. Although the coping measure used by Graves et al. (2014) is composed of approach, problem-focused, and emotion-focused subscales, the specific behaviors described in the results are descriptive of primary control coping and secondary control coping. Based on the findings, it could be hypothesized that when coping with pain, children and adolescents with SCD use primary control coping in order to change the stressor or their emotional responses, and secondary control coping is associated with less severe pain.

Links between Coping and Cognitive Functioning

The neurocognitive effects of SCD have significant implications for academic achievement and intelligence, but they may also have implications for emotional development, coping, and emotion regulation. Previous research in other pediatric populations has shown that cognitive functioning is a significant resource for adaptive coping (e.g., Campbell et al., 2009; Hocking et al., 2011; Robinson et al., 2014). For example, cognitive reappraisal relies on executive functioning and working memory, which emphasizes the ability to hold information, manipulate it, and view it from an alternative perspective. The importance of this is highlighted for children with chronic illnesses because their ability to cope with stress may be compromised by deficits in executive functioning and verbal reasoning which is a result of the illness itself.

The association between EF and coping has yet to be investigated in children and adolescents with SCD; nevertheless, there is evidence of this relationship in other pediatric samples. Campbell et al. (2009) investigated the relationship between coping and cognitive functioning in children with acute lymphocytic leukemia. They found that working memory and self-monitoring were positively associated with primary control coping and secondary control coping, and they were also negatively associated with disengagement. Cognitive flexibility and behavioral inhibition were also positively related to primary control coping, however other significant associations were only found between cognitive flexibility and secondary control coping along with behavioral inhibition and disengagement in the expected directions. Further, an intervention study by Riggs, Blair, and Greenberg (2003) showed that executive functioning, measured by inhibitory control, in elementary school children at baseline was predictive of teacher-reported behavioral change and reduction in externalizing behavior and reduced parent-reported internalizing behavior at the 2-year follow-up. By teaching coping skills to children with behavioral problems, they were also able to improve their cognitive functioning.

In addition to studies of EF and working memory, studies have also shown a relationship between verbal comprehension and emotion regulation. Language plays a critical role in the development of emotion regulation and coping strategies (Dodge & Garber, 1991). (Gallahger, 1999) described that language is necessary in “self-reflection, verbal mediation, response inhibition, and behavioral direction” (p. 5). Language processes allow children and adolescents to reflect on and regulate their emotions by engaging in internal self-speech and reappraisal along with verbal help-seeking behaviors (Kopp, 1992; Kopp, 1989). Another hypothesis about the relationship between verbal comprehension and emotional regulation focuses on modeling and the social learning aspect of coping. Children learn much of their coping skills from direct observations of caregivers and explicit teaching attempts from caregivers. Both of these social learning experiences encompass a high verbal demand and may require complex verbal reasoning abilities.

Although this relationship has not been shown in pediatric populations, researchers have found significant effects in typically developing children and children with language impairments. For example, Sala, Pons, and Molina (2014) found that verbal skills, measured with the Peabody Picture Vocabulary Test – Revised (PPVT-R; Dunn & Dunn, 1981) was associated with emotion regulation, such that higher scores were related to a greater use in seeking social support in the 3- and 4-year olds and cognitive reappraisal in 5- and 6-year olds. For young children, language skills are also positively associated with the use of distraction during stressful situations (Stansbury & Zimmermann, 1999). Another study looking at emotion regulation ratings in school-aged children with Specific Language Impairment (SLI) showed that children with SLI received significantly lower teacher-reported ratings of emotion regulation compared to students without SLI (Fujiki, Brinton, & Clarke, 2002). Although coping and emotion regulation are not interchangeable in every respect, they are very related and, depending on the researcher and study, they often share behavioral and cognitive components and strategies (Compas et al., 2014).

While there is some evidence of the relationship between coping and cognitive functioning, researchers have yet to determine how this relationship is implicated in the experience of distress in any pediatric populations.

Present Research and Hypotheses

Research has shown that children and adolescents with SCD face significant levels of stress related to their disease that is related to an increase in symptoms of distress. While the descriptive literature on levels of distress within this population have been inconsistent, there is evidence that the way children cope with disease-related stress is associated with quality of life and daily functioning. No studies in this area, however, have assessed coping using the control-based model of coping, nor have they looked at how children with SCD cope with disease-related stress outside of pain. Further, children with SCD are at risk for considerable cognitive impairment across several domains, and these deficits increase with age. Children who experience cognitive deficits as a result of the disease may have more difficulty in coping with stressful events, making them at higher risk for developing emotional problems.

The purpose of the present study is to investigate how children and adolescents with SCD cope with a broader range of disease-related stress, including but not limited to pain and daily role functioning. Coping, here, is defined as purposeful and volitional behaviors and cognitive attempts to regulate the self and the environment when under stress (e.g., Compas et al., 2001; Skinner & Edge, 1998; Eisenberg, Fabes, & Guthrie, 1997). Second, this study will examine how coping is related to symptoms of distress using a nationally represented standardized measure. Finally, I will look at how coping and distress are related to two domains of cognitive functioning (executive functioning and verbal reasoning), and determine direct and indirect associations between cognitive functioning and distress through coping. I hypothesize that:

1. There will be a positive association between cognitive function (i.e., working memory and verbal comprehension) and secondary control coping.
2. Working memory and verbal comprehension will be negatively associated with symptoms of anxiety and depression.
3. Primary control coping and secondary control coping will be negatively related to anxiety and depression, whereas disengagement will be positively associated with anxiety and depression.
4. Coping will account for a significant portion of the variance in the relationship between cognitive functioning and distress.

CHAPTER II

METHOD

Participants

Participants included 47 children and adolescents with SCD between the ages of 6 and 16 (*M* = 9.30 years, *SD* = 3.03), 57.4% male. Participants represented a variety of sickle cell disease subtypes: 68.1% were diagnosed with HbSS, which is typically regarded as the most severe type (Ashley-Kock, Yang & Olney, 2000). Another 19.1% and 10.6% were diagnosed with HbSC, and variations of S-beta thalaseemia, respectively. Results from patient's most recent MRI studies indicated that the majority of children (77.3%) displayed no evidence of an overt cerebral infarct. Of the remaining 22.7%, 6 patients presented with a history of silent stroke and 2 with a history of overt stroke, and 1 with both silent and overt stroke. Sixty-eight percent of the sample had a comorbid diagnosis of asthma. As expected, the majority of the sample (97.7%) identified as African American. With regard to school, caregivers reported that children missed a mean of 5.31 days (*SD* = 6.75) of school in the last year. Furthermore, 6.8% of the sample had repeated a grade and 22.7% received special services (e.g., Individualized Education Program, 504 plan).

Participants also included 44 primary caregivers of children and adolescents with SCD. Caregivers were primarily biological parents (n=38); the sample also included adopted parents (*n* = 1), grandparents (*n* = 3), and other primary caregivers (*n* = 2). Overall, caregivers ranged in age from 25 to 60 years old (*M* = 39.57, *SD* = 9.43), and 79.5% were female. Self-report indicated that only one caregiver (2.5%) carried their own diagnosis of sickle cell disease. Caregivers came from a range of educational background (11th grade to 3rd year of graduate school; *M* = 13.65 years of education) as well as annual family income levels (37.2% earned

$25,000 or less, 30.2% earned $25,001 to $50,000, 16.3% earned $50,001 to $75,000, 9.3% earned $75,001 to 100,000, and 7.0% earned $100,000 or above).

Procedure

Families were originally recruited to participate as part of a larger descriptive study examining the association of environmental factors of stress and parenting with cognitive functioning in children with SCD above and beyond the effect of medical characteristics. Eligibility requirements included: (a) confirmed diagnosis of sickle cell disease, (b) child age of 6-16 years at study entry, and (c) participation of a caregiver who has legal guardianship and is primarily responsible for the child. Children with a history of comorbid neurologic disorder (e.g., neurofibromatosis, lead poisoning, tuberous sclerosis) were excluded from participating. Informed consent and informed assent were obtained from caregivers and children, respectively, prior to study entry and participation. The study protocol was reviewed and approved by the Vanderbilt University Institutional Review Board.

All recruitment occurred at the Monroe Carrell Children's Hospital at Vanderbilt Sickle Cell Clinic and the Matthew Walker Comprehensive Health center, where participants received their care. Eligible families were identified by members of the pediatric hematology medical team. During routine appointments, familiar medical personnel introduced the study to caregivers. After receiving verbal consent to be approached by a member of the research team, families were given additional information and were recruited for participation if interested. During the laboratory-based study visit, children completed a brief cognitive assessment battery. Caregivers also completed a series of questionnaires assessing family sociodemographics, child coping, and child distress. Adolescents (ages 10 to 16 years old) were also asked to complete one questionnaire on coping after their testing was complete. Families received compensation at the end of the visit.

Measures

Demographic and medical data. Parents provided demographic information, including age, education level, race, family income, and marital status. Parents gave permission for the research staff to access medical data, where the child's hemoglobin and stroke status were extracted.

Children's verbal reasoning. Children with SCD completed the Wechsler Abbreviated Scale of Intelligence – Second Edition Verbal Comprehension Index (WASI-II; Wechsler, 2011). The WASI-II is widely used to assess intelligence in children and adults. The Verbal Comprehension Index (VCI) is comprised of the Vocabulary and Similarities subtests and is designed to measure verbal comprehension.

Children's working memory. Children were also administered subtests that make up the Working Memory Index (WMI) from the Wechsler Intelligence Scale for Children – Fourth Edition (WISC-IV; Wechsler, 2003). The WISC-IV is the benchmark test used to assess intelligence in children. The WMI, composed of Digit Span and Letter-Number Sequencing subtests, is a measure of the ability to concentrate, sustain attention, and exert mental control.

Children's coping. The Responses to Stress Questionnaire-Sickle Cell Disease version (RSQ-SC; Connor-Smith et al., 2000) was used to obtain adolescents' self-report and parent reports of their children's coping with SCD. The RSQ-SC version includes a list of 8 SCD-related stressors (e.g., having sickle cell pain crises, missing school days, concerns about the future), and 57 items reflecting voluntary (coping) and involuntary (automatic) stress responses of children/adolescents in response to cancer-related stressors. Because this study was focused on children's coping responses, only the three voluntary coping scales are reported. The coping scales include primary control coping (i.e., problem-solving, emotional modulation, emotional expression), secondary control coping (i.e., acceptance, cognitive restructuring, positive thinking, distraction), and disengagement (i.e., avoidance, denial, wishful thinking). Using the standard method for scoring the RSQ, and to control for response bias and individual differences in base rates of item endorsement, proportion scores were calculated by dividing the total score for each factor by the total score for the entire RSQ.

In the current sample, internal consistencies of children's self-reports (ages 10 to 16) were primary control, $\alpha = .86$; secondary control, $\alpha = .80$; and disengagement, $\alpha = .69$. Internal consistencies for parent reports, respectively, were primary control, $\alpha = .84$; secondary control, $\alpha = .91$; and disengagement, $\alpha = .84$. The factor structure of the RSQ has been supported in confirmatory factor analytic studies with children and adolescents from a wide range of ethnic and cultural backgrounds coping with a variety of stressors (e.g., Benson et al., 2011; Compas et al., 2006; Connor-Smith et al., 2000; Wadsworth et al., 2004; Yao et al., 2010).

Children's emotional distress. Child and adolescent symptoms of distress were assessed using mother and father reports of anxiety and depression on the Child Behavior Checklist (CBCL). Reliability and validity are established for the CBCL, and normative *T* scores are derived from a parents' report on a nationally representative sample of children and youth ages 6 to 17 years old (Achenbach & Rescorla, 2001). Depressive symptoms were measured with the Affective Problems subscale, anxiety symptoms were measures with the Anxiety Problems subscale, and mixed Anxiety-Depression was measured using the anxious-depressed subscale.

Statistical Analyses

Descriptive statistics for sample demographic information, along with means and standard deviation for cognitive domains, distress levels, and coping were calculated. Additionally, Pearson correlation analyses were performed to determine significant bivariate associations between the measures of cognitive function, coping, and distress. Multiple linear regressions were done to examine the association of cognitive functioning with coping, cognitive functioning on distress, and coping on distress while controlling for age and relevant medical characteristics. Finally, to evaluate the variance in the relationship between cognitive domains and distress that is accounted for by coping, model 4 of PROCESS macro for SPSS was used (Hayes, 2013). This is based on Ordinary Least Squares regression and incorporates a parametric bootstrapping procedure that provides confidence intervals on total, direct, and indirect effects. The current analyses were conducted with a 95% confidence interval for the indirect effect with 1000 bootstrap samples. An indirect effect contributes significantly to the model estimation when the confidence interval of the indirect path does not contain zero (Hayes, 2009). Similar analyses have been used with pediatric oncology (Harper, Peterson, & Uphold, 2013; Murphy et al., 2015).

CHAPTER III

RESULTS

Outliers. After assessing the distributions of the distress variables, one participant that produced extreme scores on all three measures of distress (>2 *SD* on Anxiety Problems and mixed Anxious-Depressed, and >1 *SD* on Affective Problems subscales) was excluded in the bivariate and regression analyses.

Descriptive Statistics

Mean (*M)* scores and standard deviations (*SD*) for both domains of cognitive functioning, coping, and measures of distress are reported in Table 2. Scores were significantly lower than the standardized mean of 100 for both working memory, $t(46) = -3.36$, $p = .002$, $d = .47$, and verbal comprehension, $t(46) = -3.39$, $p < .001$, $d = .49$. Reports of child emotional distress on the Affective Problems scale showed a medium effect for elevated depressive symptoms, $t(42) = 4.93$, $p < .001$, $d = .66$. *T*-scores for the parent reports of child anxiety symptoms and mixed anxiety and depression were also slightly above the normative mean of 50 (anxiety symptoms, $t(42) = 3.94$, $p < .001$, $d = .45$; anxious-depressed, $t(42) = 3.15$, $p = .003$, $d = .39$). *M*s and *SD*s of ratio scores for parent- and self-reported child coping are also described in Table 2; however, due to the small sample of adolescents who were able to provide self-reports (age ≥ 10, $n = 16$), parent-reports of child coping were used in all further analyses.

Bivariate Correlations

Bivariate Pearson correlations between cognitive function domains, emotional distress, and coping are reported in Table 3. Looking at the relationship between cognitive functioning and coping, verbal comprehension was significantly associated with secondary control coping ($r = .42$, $p = .006$), such that higher scores for verbal comprehension were associated with more use of reappraisal, acceptance, and distractions when coping with stress related to SCD. Working memory, however, was not related to secondary control coping (*r* = .14, *p* = .362). Finally, neither verbal comprehension nor working memory were associated with primary control coping or disengagement.

Working memory was significantly and negatively associated with depressive symptoms (*r* = -.38, *p* = .012). Lower scores on working memory were related to higher reports of depressive symptoms. Verbal comprehension was not related to depressive symptoms (*r* = -.14, *p* = .395). Finally, neither working memory nor verbal comprehension were related to reports of anxiety symptoms or mixed anxiety and depression.

Bivariate analyses showed that secondary control coping was significantly and negatively associated with depressive symptoms (*r* = -.35, *p* = .022) and its negative association with anxiety symptoms approached significance (*r* = -.27, *p* = .081). In addition to this, primary control coping was related to mixed anxiety and depression (*r* = -.34*, p* = .031), whereas secondary control coping was not (*r* = -.13, *p* = .426). Associations between disengagement and distress were nonsignificant, yet all were in the expected positive direction.

Linear Regression Analyses

A series of linear regression analyses were conducted to better understand how cognitive functioning and coping might account for the variance in distress, while controlling for age, hemoglobin level at closest clinic appointment, and history of stroke. Given the pattern of the bivariate correlations reported above, regression analyses were only conducted with secondary control coping as the primary outcome for testing hypothesis 1, and depressive symptoms as the outcome for testing hypotheses 2 and 3.

Cognitive functioning and coping with SCD. Table 4 describes the results of a stepwise linear regression analysis of child cognitive functioning predicting secondary control coping. Due to the emphasis on EF and its relationship with coping in the current literature, working memory was entered in to the equation in the first step with age and relevant medical characteristics. Verbal comprehension was then added to the equation in Step 2 in order to assess the unique and shared contribution of working memory versus verbal comprehension in the prediction of secondary control coping. Results from Step 1 showed that working memory was not significantly predictive of levels of secondary control coping (B = .00, β = .10, *p* = .575). Step 2 showed the effect of each cognitive functioning domain while controlling for medical characteristics. Verbal comprehension was positively predictive of secondary control coping (B = .00, β = .51, *p* = .007) whereas working memory was not (B = -.00, β = -.21, *p* = .273).

Cognitive functioning and distress. The second aim of the study was to investigate how cognitive functioning predicted levels of distress in children with SCD. As shown in Table 5, working memory was a significant predictor of depressive symptoms when controlling for medical characteristics in Step 1 (B = -.23, β = -.42, *p* = .012), and it remained significant after adding verbal comprehension in Step 2 (B = -.27, β = -.51, *p* = .012). Higher scores on the WMI predicted lower parent-reports of children's depressive symptoms. Verbal comprehension was not a significant predictor of depressive symptoms (B = .10, β = .15, *p* = .422).

Secondary control coping and distress. Results of the stepwise linear regression of child coping predicting depressive symptoms are reported in Table 6. Secondary control coping significantly predicted depressive symptoms while controlling for medical factors (B = -41.23, β = -.36, *p* = .032), and this relationship approached significance when adding primary control coping and disengagement to the model in Step 2 (B = -44.78, β = -.39, *p* = .060). Neither primary control coping (B = -53.69, β = -.25, *p* = .191) nor disengagement (B = -12.65, β = -.05, *p* = .838) was a significant predictor of depressive symptoms.

Secondary control coping in the relationship between cognitive functioning and distress. The direct and indirect paths for the association between verbal comprehension on depressive symptoms through coping are shown in Figure I. In this model, there was a significant path coefficient from verbal comprehension to secondary control coping (path a; B = .002, *p* = .006), and the path coefficient from secondary control coping to depressive symptoms was also significant (path b; B = -46.92, *p* = .04). While there was not a direct association between verbal comprehension and depressive symptoms, shown by path c (B = -.09, *p* = .39) and path c' (B = .01, *p* = .93) in Figure I, the PROCESS macro analysis showed that there was a significant indirect relationship, such that secondary control coping accounted for a significant portion of the variance in the association between verbal comprehension and depressive symptoms (-.15, Boot SE = .08, 95% CI = -.36 to -.03). The same pattern of significant associations was found when this model controlled for hemoglobin level at clinic, history of stroke, and age.

Figure II shows coefficients for the direct and indirect associations between working memory and depressive symptoms through coping. Here, there was no association between working memory and secondary control coping (path a; B = .00, *p* = .362). Consistent with the model presented in Figure I., there was a significant path coefficient for the relationship between secondary control coping and depressive symptoms (path b; B = -39.64, *p* = .039). Finally, while there was not an indirect association through coping (B = -.04, Boot SE = .04, 95% CI = -.15 to .03), there was a direct relationship between working memory and depressive symptoms as shown by path c (B = -.21, *p* = .012) and path c' (B = -.18, *p* = .021). The same pattern of significant paths was found when hemoglobin, history of stroke, and age were included in the model as covariates.

CHAPTER IV

DISCUSSION

Children and adolescents with SCD are faced with a significant amount of stress related to symptoms of the illness, pain crises, intensive and prolonged treatments, disruptions in daily functioning, and uncertainty about the future. Understanding how children cope with stress, along with understanding the influences of cognitive abilities, is important to crafting valuable interventions for this population. The purpose of this study was to investigate the relationship between cognitive functioning, coping, and distress in a sample of children with SCD.

Previous research on coping in this population has focused primarily on coping with pain rather than coping with stress related to having SCD, and they also used Gil's (1991) model of coping that featured coping attempts, negative thinking, and passive adherence. Within this study, coping was defined here as purposeful and volitional behaviors and cognitive attempts to regulate the self and the environment, and these coping efforts are organized around perceived and actual levels of personal control (Compas et al., 2001, 2012). While coping attempts and passive adherence from Gil's (1991) model aligns with this definition, negative thinking does not. Further, few studies have investigated how coping is related to internalizing problems, and within those that have looked at this relationship only found effects for negative thinking, which is not a purposeful or volitional attempt. This, and the uncontrollable nature of the stressors that children with SCD face, suggest that the control-model of coping may a better method of assessing coping within this population. Finally, no study has investigated how cognitive functioning is related to both coping and distress in children and adolescents with SCD. The current multimethod study presented new findings related to coping in pediatric SCD using the control model of coping, and the results presented here identify potential paths through which cognitive functioning and distress are related. Results pose important clinical and research implications related to children and adolescents with SCD.

Mean scores on working memory and verbal comprehension composites were significantly lower than the standardized mean, yet they were higher than scores reported in previous studies. On average children with SCD scored 93.09 on the WISC-IV WMI and 93.34 on the VCI, which are nearly 7 points below the normative mean for each composite. Yarboi et al. (2015) assessed deficits in EF in children with SCD, and they showed that the effect sizes ranged from -.02 to -.73 on tests from the D-KEFS. Other studies assessing working memory using the Digit Span subtest from a Wechsler test have reported that children with SCD obtain mean standard scores between 8 and 9 on Digit Span Forward and between 5 and 7.4 on Digit Span Backward (Hijmans et al., 2011; Schatz & Roberts, 2005). Although studies within this literature utilize a wide range of measures to assess EF, scores for children in the current sample are somewhat higher than previous reports when comparing the effect sizes across all of these studies.

Hijmans et al. (2011) found that in a sample of children with severe forms of SCD (i.e, HbSS or HbB^0 Thalaseemia) the average Verbal IQ score was 83 (SD = 12.1) on the WISC-III. Other findings on verbal IQ in pediatric SCD have were consistent with this, producing average scores of 80.33 on the WISC-III and 87.7 on the WJ-R (Schatz & Roberts, 2005; Steen et al., 2005). There are two possible explanations for the higher score in the current sample. First, the current sample included all genotypes of SCD, including HbSC and $HbS\beta^+$ Thalaseemia, meaning the range of biological risks for cognitive deficits are likely to be wider in this sample. Second, only 14% of the sample in Hijmans et al. (2011) were receiving active treatment, whereas 100% of children in the current study were receiving either hydroxyurea or had a chronic transfusion plan. It has been shown that children with SCD taking oral hydroxyurea score higher on standardized assessments of verbal comprehension and other cognitive domains compared to children who are not on any active treatment (Puffer, Schatz, & Roberts, 2007). Further, Yarboi et al. (2015) found that the average score for the WASI Verbal IQ composite was 94.97 (SD = 15.63), in an all-inclusive sample of children with SCD that were receiving active treatments, which aligns closely with the findings presented here.

Reported levels of distress within this sample suggests that children with SCD experience mild symptoms of anxiety and moderate depressive symptoms. The mean *T* score for depressive symptoms was 55.95, which demonstrates a medium effect (Cohen, 1997), and parents also reported a mean *T* score of 53.74 for child anxiety problems and 53.42 for child mixed anxious-depressed symptoms. These scores are comparable to that of previous literature within this population. Trzepacz et al. (2004) also reported levels of internalizing in children with SCD using parent reports on the CBLC. In that study, parents reported an average score of 56.79 for Withdrawn, 59.76 for somatic complaints, and 55.46 for anxious/depressed (Trzepacz et al.). While the researchers did not report data on affective or anxiety problems, their finding on mixed anxiety and depression is similar to the mean found in the present study. Lemanek et al. (1986) also reported similar levels of depressive symptoms using the CDI, and they found higher scores for internalizing problems using the CBCL. As noted before, the literature on internalizing symptoms in this population is inconsistent (Benton et al., 2007). Nevertheless, the results of the current study provide evidence that children and adolescents with SCD may have mild to moderately elevated symptoms of anxiety and depression.

Coping with SCD-related stress was assessed using the control-based model of coping, and primary control coping, secondary control coping, and disengagement were all presented as proportion scores. When coping with the stress of SCD (which includes uncertainty, pain crises, disruptions in daily role functioning), parents reported that children used secondary control coping more than primary control coping and disengagement. This finding is consistent previous literature that used the control-based model of coping within other pediatric populations. For example, Compas et al. (2014) discussed how children and adolescents diagnosed with cancer coped with the stress of their illness. Parent and child-reports of coping showed that the proportions scores for primary control coping ranged from .18 to .19 and scores for secondary control coping ranged from .28 to .29. Therefore, reports from both parents and children were consistent in showing that children used secondary control coping at a higher proportion than primary control coping. This pattern was also shown in samples of children with diabetes and other pediatric populations (Compas et al., 2014; Jaser & White, 2011). All of these findings highlight the use of cognitive reappraisal, acceptance, and distraction when dealing with the many uncontrollable sources of stress related to childhood illness.

The current study assessed how children with SCD cope with a range of sickle cell-related stressors, whereas much of the previous literature has only assessed how this population copes with SCD-related pain. Although pain was listed as a stressor alongside items related to uncertainty and disruptions in daily role functioning, adaptive coping may be different within both situations. Coping is to some degree context specific, and the outcome of a coping mechanism is dependent on its fit to the stressor at hand. For example, one study that used the Pediatric Pain Coping Questionnaire found that children and adolescents used positive approach coping (i.e., seeking information and support for pain) more than problem-focused or emotion-focused avoidance (Graves & Jacob, 2014). Previous literature using the CSQ model of coping reported that children with SCD use passive adherence (i.e., behaviors typically recommended by healthcare professions to decrease, manage, or control pain) when coping with the pain crises most often, followed by negative thinking, and coping attempts (Gil et al., 1991). Considering the control-based model of coping, the components of positive approach coping and passive adherence coping may reflect behaviors within primary control coping.

Although it was not a SCD sample, Thomsen et al. (2002) used the control-based model of coping to assess pain coping and distress in children with recurrent abdominal pain (RAP). They found that when coping with the stress of pain the proportion score for primary control coping was .21 and the proportion score for secondary control coping was also .21. This could imply that when coping with the stress of pain, children with RAP equally relied on problem-solving skills and strategies related to cognitive reappraisal and acceptance. Pain as a stressor within pediatric populations could be viewed as a combination of both a controllable and uncontrollable situation. The diagnosis of the disorder or disease is uncontrollable, which means that secondary control coping mechanisms would be the most adaptive. However, problem-solving and adherence behaviors are also important when managing the pain itself which could appear to be more controllable than uncontrollable. Together with the pain coping literature in pediatric SCD, it could be hypothesized that children with SCD use primary control coping to cope with pain. If so, it could suggest that primary control coping is implicated more in coping with SCD-related pain compared to coping with disease-related stress.

In addition to determining descriptive findings on cognitive functioning, coping, and distress, the aim of this study was to test four primary hypotheses about coping and distress in pediatric SCD. First, we hypothesized a positive association between cognitive function and secondary control coping. This hypothesis was partially supported in that bivariate correlations showed that verbal comprehension was associated with coping. Further, results showed that even when controlling for age, medical characteristics, and scores for working memory, verbal comprehension remained a significant predictor of secondary control coping. Higher ability in verbal comprehension and concept formation was associated with a higher use of reappraisal, positive thinking, and distraction when coping with the stress of SCD. This finding was consistent with the previous literature on verbal skills and emotion regulation, and it supports the hypothesis that language and verbal comprehension play a crucial role in emotion regulation and coping strategies, particularly when it comes to cognitive reappraisal and positive thinking. In addition to other sequelae of cognitive deficits in this domain, impaired in verbal comprehension in children with SCD may have downstream effects on how they are able to cope with the high levels of uncontrollable stress related to the disease itself.

Given the previous literature on this topic, it was not expected, however, that working memory would not be related to coping. Findings within other pediatric populations have been able to show this relationship between EF and coping (e.g., Campbell et al., 2009), and it is unclear whether results from the present study is a reflection of the sample or of the pediatric SCD population. Due to the consistent literature in both normative and pediatric populations, I hypothesize that this is a result of low power within this sample and not a reflection of the population as a whole.

While unable to replicate the association between EF and coping, interesting findings on the relationship between working memory and distress were reported. The second hypothesis, which stated that cognitive functioning would be significantly related to distress, was partially supported. Working memory was related to depressive symptoms whereas verbal comprehension was not. Further, neither working memory nor verbal comprehension were related to anxiety symptoms or the mixed anxiety and depression. When looking at the two domains of cognitive functioning as predictors within a single model that controlled for age and medical characteristics, working memory remained the only significant predictor of depressive symptoms suggesting that it accounts for a unique portion the variance in depressive symptoms. This highlights the importance of working memory as a component of executive function in the experience of depressive symptoms within this population, and it also replicates findings from studies in general populations with depression as well (Snyder, 2013).

In support of the third hypothesis of this study, secondary control coping was significantly associated with depressive symptoms above and beyond medical characteristics associated with disease severity. Both bivariate and regression analyses showed that coping with stress related to having SCD using reappraisal, acceptance, and distraction was significantly related to fewer depressive symptoms, suggesting that coping with the uncontrollable sources of stress is important when adjusting to SCD.

The association between secondary control coping and internalizing symptoms has been reliably shown within previous pediatric literature in children with cancer and recurrent abdominal pain (Compas et al., 2014; Thomsen et al., 2002), yet this finding also adds to the current literature on coping and adjustment in pediatric SCD that has been very limited in focus. Only three previous studies have examined the relationship between coping and measures of distress, and all of them used Gil and Thompson's model of pain coping. Within this model, effects have yet to be found for coping attempts, which is composed of behaviors relevant to secondary control coping, and only positive associations were found between negative thinking and passive adherence with internalizing symptoms and adjustment problems (Barakat et al., 2007; Gil et al., 1991; Thompsen et al., 1993). As previously mentioned, negative thinking does not align with the definition of coping used here because it is an unintentional effect of stress rather than an active attempt to regulate the self or environment. Further, when describing the reported association between passive adherence and internalizing symptoms, it could be theorized that it is the symptoms that lead to an increase use of adherence behaviors rather than the other way around. The difference in findings could either be contributed to a qualitative difference in how children with SCD cope with stress compared to coping with pain, or it could be a function of the reliability and structure of the two coping measures.

Finally, the fourth hypothesis was also partially supported. Our analyses showed that working memory only had a direct association with depressive symptoms, whereas verbal comprehension only showed an indirect relationship with these symptoms through secondary control coping. In other words, the association between verbal comprehension and depressive symptoms is only explained by their mutual association with secondary control coping. This finding has at least two important implications. First, cognitive impairment in children with SCD, which occurs as a function of the illness itself and other demographically-relevant factors, is related to emotional distress within this sample. Second, how a child copes with the stressors associated with SCD is relevant and important in the relationship between cognitive functioning psychological adjustment. Interestingly, previous studies have found both a direct and indirect association for EF in a pediatric population (e.g., Campbell et al., 2009), and no study has looked at how verbal comprehension could be indirectly associated with depressive symptoms in general.

Previous studies within this population have emphasized the importance of cognitive deficits for academic achievement. However, the results from this study shows that in addition to their association with achievement, deficits in working memory and verbal comprehension are also associated influence how children cope with the stress of the illness and their emotional wellbeing as well. Further, studies have shown that deficits in cognitive functioning increase with age (Schatz et al., 2002). While this finding and the results of the current study show clear clinical implications for children and adolescents, SCD is a lifelong disorder and these effects could influence emotional wellbeing well into adulthood. Understanding the relationship between cognitive functioning, coping, and distress further emphasize the necessity for early intervention within this population.

Overall, the current study used a multimethod approach using data from validated standardized assessments, nationally standardized measures of distress, and parent-reported questionnaires to in a comprehensive sample of children with SCD receiving the most up-to-date treatments. Several novel findings were presented. Children with SCD experience increased levels of depressive symptoms relative to nationally standardized averages, and they also show deficits in both working memory and verbal reasoning. Further, these deficits are related to increased symptoms of depressive symptoms. However, the way children cope with the many uncontrollable stressors related to their illness is not only associated with depressive symptoms, but it also explains a relationship between verbal comprehension and emotional distress.

The limitations of the study will be important to address in future research. First, the study was cross-sectional, and therefore temporal precedence among the variables was not achieved, meaning mediation could not be tested. It will be important to use a longitudinal design to determine how cognitive functioning, coping, and emotional distress in children with SCD are related across time. In addition to establishing temporal precedence, a longitudinal study will also be able to determine the direction of the associations. Second, due to limitations in sample size and age-restrictions on measures, only parent reports of child coping and emotional distress were assessed. Future research must include both parent and adolescent self-reports of coping and distress, and new methods must be used to determine self-reported levels of these constructs within younger children. An increased sample size will also enable researchers to examine a moderator effect for working memory and verbal comprehension on coping and distress. Secondary control coping may be most effective for children who receive high scores on both working memory and verbal comprehension. Finally, the assessment of stress using questionnaires have been recently criticized within the literature. While this study did not directly include variables related to stress, new research on this subject must consider that stress is a highly subjective experience, and in order to get a more reliable understanding of the stressors facing the population at hand, structured interviews should be given. These limitations should be addressed in future research related to cognitive functioning, coping, and distress in children and adolescents with SCD.

In summary, this study poses potential clinical implication for teaching children with SCD coping strategies related to secondary control coping in order to help abate another negative sequelae of cognitive impairments in this populations.

REFERENCES

Achenbach, T. M., & Rescorla, L. A. (2001). *Manual for the ASEBA school-age forms and profiles*. Burlington, VT: University of Vermont, Research Center for Children, Youth, and Families.

Adams, R., McKie, V., Nichols, F., Carl, E., Chang, D.-L., KcKie, K., … Hess, D. (1992). The Use of Transcranial Ultrasonography to Predict Steoke in Sickle Cell Disease. *The New England Journal of Medicine*, *327*(10), 685–691.

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

Barakat, L. P., Patterson, C. A., Tarazi, R. A., & Ely, E. (2007). Disease-related parenting stress in two sickle cell disease caregiver samples: Preschool and adolescent. *Families, Systems, & Health*, *25*(2), 147–161.

Benson, M. A., Compas, B. E., Layne, C. M., Vandergrift, N., Pašalić, H., Katalinksi, R., & Pynoos, R. S. (2011). Measurement of post-war coping and stress responses: A study of Bosnian adolescents. *Journal of Applied Developmental Psychology*, *32*(6), 323–335.

Benton, T., Ifeagwu, J., & Smith-Whitley, K. (2007). Anxiety and depression in children and adolescents with sickle cell disease. *Current Psychiatry Reports*, *9*, 114–121.

Bernaudin, F., Verlhac, S., & Freard, F. (2000). Multicenter prospective study of children with sickle cell disease: radiographic and psychometric correlation. *Journal of Child Neurology*, 333–343.

Campbell, L. K., Scaduto, M., Van Slyke, D., Niarhos, F., Whitlock, J. A., & Compas, B. E. (2009). Executive function, coping, and behavior in survivors of childhood acute lymphocytic leukemia. *Journal of Pediatric Psychology*, *34*(3), 317–327.

Cohen, J. (1997). *Statistical power analysis for the behavioral sciences*. New York, NY: Academic Press.

Compas, B. E., Boyer, M. C., Stanger, C., Colletti, R. B., Thomsen, A. H., Dufton, L. M., & Cole, D. A. (2006). Latent variable analysis of coping, anxiety/depression, and somatic symptoms in adolescents with chronic pain. *Journal of Consulting and Clinical Psychology*, *74*(6), 1132–1142.

Compas, B. E., Champion, J. E., Forehand, R., Cole, D. A., Reeslund, K. L., Fear, J., … Roberts, L. (2010). Coping and parenting: Mediators of 12-month outcomes of a family group cognitive-behavioral preventive intervention with families of depressed parents. *Journal of Consulting and Clinical Psychology*, *78*(5), 623–634.

Compas, B. E., Connor-Smith, J. K., Saltzman, H., Thomsen, A. H., & Wadsworth, M. E. (2001). Coping with stress during childhood and adolescence: problems, progress, and potential in theory and research. *Psychological Bulletin*, *127*(1), 87–127.

Compas, B. E., Desjardins, L., Vannatta, K., Young-Saleme, T., Rodriguez, E. M., Dunn, M., … Gerhardt, C. A. (2014). Children and adolescents coping with cancer: self- and parent reports of coping and anxiety/depression. *Health Psychology*, *33*(8), 853–61.

Compas, B. E., Jaser, S. S., Dunbar, J. P., Watson, K. H., Bettis, A. H., Gruhn, M. A., & Williams, E. K. (2014). Coping and emotion regulation from childhood to early adulthood: Points of convergence and divergence. *Australian Journal of Psychology*, *66*(2), 71–81.

Compas, B. E., Jaser, S. S., Dunn, M. J., & Rodriguez, E. M. (2012). Coping with chronic illness in childhood and adolescence. *Annual Review of Clinical Psychology*, *8*, 455–80.

Connor-Smith, J. K., & Calvete, E. (2004). Cross-cultural equivalence of coping and involuntary responses to stress in Spain and the United States. *Anxiety, Stress, and Coping*, *17*, 163–185.

Connor-Smith, J. K., Compas, B. E., Wadsworth, M. E., Thomsen, A. H., & Saltzman, H. (2000). Responses to stress in adolescence: measurement of coping and involuntary stress responses. *Journal of Consulting and Clinical Psychology*, *68*(6), 976–992.

Delis, D. C., Kaplan, E., & Kramer, J. H. (2001). *Delis-Kaplan Executive Function System (D-KEFS)*. San Antonio, TX: The Psychological Corporation.

Den Hartog, H. M., Derix, M. M. A., Van Bemmel, A. L., Kremer, B., & Jolles, J. (2003). Cognitive functioning in young and middle-aged unmedicated out-patients with major depression: testing the effort and cognitive speed hypotheses. *Psychological Medicine*, *33*(8), 1443–1451.

Dodge, K. A., & Garber, J. (1991). Domains of emotion regulation. In *The development of emotion redulation and dysregulation* (pp. 3–11). Cambridge, UK: Cambridge University Press.

Dunn, M., & Dunn, L. M. (1981). *Peabody Picture Vocabulary Test - Revised.* Circle Pines, MN: American Guidance Service.

Eisenberg, N., Fabes, R. A., & Guthrie, I. (1997). Coping with stress: The roles of regulation and development. In J. N. Sandler & S. A. Wolchik (Eds.), *Handbook of children's coping with common stressors: Linking theory, research, and intervention* (pp. 41–70). New York: Plenum.

Fioravanti, M., Carlone, O., Vitale, B., Cinti, M. E., & Clare, L. (2005). A meta-analysis of cognitive deficits in adults with a diagnosis of schizophrenia. *Neuropsychology Review*, *15*(2), 73–95.

Fisk, J. E., & Sharp, C. a. (2004). Age-related impairment in executive functioning: updating, inhibition, shifting, and access. *Journal of Clinical and Experimental Neuropsychology*, *26*(7), 874–90.

Friedman, N. P., Miyake, A., Corley, R. P., Young, S. E., DeFries, J. C., & Hewitt, J. K. (2006). Not all executive functions are related to intelligence. *Psychological Science*, *17*(2), 172–179.

Friedman, N. P., Miyake, A., Young, S. E., Defries, J. C., Corley, R. P., & Hewitt, J. K. (2008). Individual differences in executive functions are almost entirely genetic in origin. *Journal of Experimental Psychology: General*, *137*(2), 201–25.

Fujiki, M., Brinton, B., & Clarke, D. (2002). Emotion regulation in children with specific language impairment. *Language, Speech, and Hearing Services in Schools*, *33*(2), 102–111.

Gallahger, T. M. (1999). Interrelationships among children's language, behavior, and emotional problems. *Topics in Language Disorders*, *19*(2), 1–15.

Gil, K. M., Anthony, K. K., Carson, J. W., Redding-Lallinger, R., Daeschner, C. W., & Ware, R. E. (2001). Daily coping practice predicts treatment effects in children with sickle cell disease. *Journal of Pediatric Psychology*, *26*(3), 163–173.

Gil, K. M., Carson, J. W., Porter, L. S., Ready, J., Valrie, C., Redding-Lallinge, R., & Daeschner, C. (2003). Daily stress and mood and their association with pain, health-care use, and school activity in adolescents with sickle cell disease. *Journal of Pediatric Psychology*, *28*(5), 363–373.

Gil, K. M., Edens, J. L., Wilson, J. J., Raezer, L. B., Kinney, T. R., Schultz, W. H., & Daeschner, C. (1997). Coping strategies and laboratory pain in children with sickle cell disease. *Annals of Behavioral Medicine*, *19*(1), 22–29.

Gil, K. M., Thompson, R. J., Keith, B. R., Tota-faucette, M., Noll, S., & Kinney, T. R. (1993). Sickle cell disease pain in children and adolescents: Change in pain frequency and coping strategies over time. *Journal of Pediatric Psychology*, *18*(5), 621–637.

Gil, K. M., Williams, D. A., Thompson Jr., R. J., & Kinney, T. R. (1991). Sickle cell disease in children and adolescents: the relation of child and parent pain coping strategies to adjustment. *Journal of Pediatric Psychology*, *16*(5), 643–663.

Goel, V., & Grafman, J. (1995). Are The Frontal Lobes Implicated in "Planning" Functions? Interpreting Data From the Tower of Hanoi. *Neuropsychologia*, *33*(5), 623–642.

Graves, J. K., & Jacob, E. (2014). Pain, coping, and sleep in children and adolescents with sickle cell disease. *Journal of Child and Adolescent Psychiatric Nursing*, *27*(3), 109–120.

Harper, F. W., Peterson, A. M., & Uphold, H. (2013). Longitudinal study of parent caregiving self-efficacy and parent stress reactions with pediatric cancer treatment procedures. *Psycho-Oncology*, *22*(7), 1658–1664.

Hassell, K. L. (2010). Population Estimates of Sickle Cell Disease in the U.S. *American Journal of Preventive Medicine*, *38*(4), S512–S521.

Hayes, A. F. (2009). Beyond Baron and Kenny: Statistical mediation analysis in the new millennium. *Communication Monographs*, *76*(4), 408–420.

Hayes, A. F. (2013). *An introduction to mediation, moderation, and conditional process analysis: A regression-based approach*. New York, NY: Guilford Press.

Hedden, T., & Yoon, C. (2006). Individual differences in executive processing predict susceptibility to interference in verbal working memory. *Neuropsychology*, *20*(5), 511–28.

Hertel, P. T., & Gerstle, M. (2003). Depressive deficits in forgetting. *Psychological Science*, *14*(6), 573–578.

Hijmans, C., Fijnvandraat, K., Grootenhuis, M., van Geloven, N., Heijboer, H., Peters, M., & Oosterlaan, J. (2011). Neurocognitive deficits in children with sickle cell disease: A comprehensive profile. *Pediatric Blood & Cancer*, *56*(5), 783–788.

Hildenbrand, A. K., Barakat, L. P., Alderfer, M. A., & Marsac, M. L. (2013). Coping and coping assistance among children with sickle cell disease and their parents. *Journal of Pediatric Hematology and Oncology*, 37(1), 25–34.

Hill, C. M., Hogan, A. M., Onugha, N., Harrison, D., Cooper, S., McGrigor, V. J., … Kirkham, F. J. (2006). Increased cerebral blood flow velocity in children with mild sleep-disordered breathing: a possible association with abnormal neuropsychological function. *Pediatrics*, *118*(4), e1100–e1108.

Hocking, M. C., Barnes, M., Shaw, C., Lochman, J. E., Madan-Swain, A., & Saeed, S. (2011). Executive function and attention regulation as predictors of coping success in youth with functional abdominal pain. *Journal of Pediatric Psychology*, *36*(1), 64–73.

Hollocks, M. J., Kok, T. B., Kirkham, F. J., Gavlak, J., Inusa, B. P., DeBraun, M. R., & de Haan, M. (2012). Nocturnal oxygen desaturation and disordered sleep as a potential factor in executive dysfunction in sickle cell anemia. *J Int Neuropsychol Soc*, *18*(1), 186–173.

Holmes, A., & Wellman, C. L. (2009). Stress-induced prefrontal reorganization and executive dysfunction in rodents. *Neuroscience and Biobehavioral Reviews*, *33*(6), 773–783.

Hudziak, J. J., Achenbach, T. M., Althoff, R. R., & Pine, D. S. (2007). A dimensional approach to developmental psychopathology. *International Journal of Methods in Psychiatric Research*, *16*(S1), S16–S23.

Jaser, S. S., & White, L. E. (2011). Coping and resilience in adolescents with type 1 diabetes. *Child: Care, Health and Development*, *37*, 335–342.

King, A. A., Strouse, J. J., Rodeghier, M. J., Compas, B. E., Casella, J. F., Mckinstry, R. C., … Debaun, M. R. (2014). Parent education and biologic factors influence on cognition in sickle cell anemia. *American Journal of Hematology*, *89*(2), 162–167.

Kopp, C. B. (1989). Regulation of distress and negative emotions: A developmental view. *Developmental Psychology*, *25*(3), 343–354.

Kopp, C. B. (1992). Emotional distress and control in young children. *New Directions for Child Development*, (55), 41–56.

Kovaks, M. (1981). Rating scales to assess depression in school-aged children. *Acta Paedopsychiatrica*, *46*, 991–994.

Kumar, S., Powars, D., Allen, J., & Haywood, L. J. (1976). Anxiety, self-concept, and personal and social adjustments in children with sickle cell anemia. *The Journal of Pediatrics*, *88*(5), 859–863.

Kwiatkowski, J. L., Zimmerman, R. A., Pollock, A. N., Seto, W., Smith-Whitley, K., Shults, J., … Ohene-Frempong, K. (2009). Silent infarcts in young children with sickle cell disease. *British Journal of Haematology*, *146*(3), 300–305.

Lemanek, K. L., Moore, S. L., Gresham, F. M., Williamson, D. A., & Kelley, M. L. (1986). Psychological adjustment of children with sickle cell anemia. *Journal of Pediatric Psychology*, *11*(3), 397–410.

Matthews, A., & MacLeod, C. (1994). Cognitive approaches to emotion and emotional disorders. *Annual Review of Psychology*, *45*, 25–50.

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.

Miyake, A., Friedman, N. P., Emerson, M. J., Witzki, a H., Howerter, A., & Wager, T. D. (2000). The unity and diversity of executive functions and their contributions to complex “Frontal Lobe” tasks: a latent variable analysis. *Cognitive Psychology*, *41*(1), 49–100.

Moran, T. P. (2016). Anxiety and working memory capacity: A meta-analysis and narrative review. *Psychological Bulletin*, *142*(5), 831–864.

Morgan, S. A., & Jackson, J. (1986). Psychological and social concomitants of sickle cell anemia in adolescents. *Journal of Pediatric Psychology*, *11*(3), 429–440.

Murphy, L. K., Rodriguez, E. M., Schwartz, L., Bemis, H., Desjardins, L., Gerhardt, C. A., … E, C. B. (2015). Longitudinal association among maternal communication and adolescent posttraumatic stress symptoms after cancer diagnosis. *Psycho-Oncology*.

Needleman, J. P., Franco, M. E., Varlotta, L., Reber-Brodecki, D., Bauer, N., Dampier, C., & Allen, J. L. (1999). Mechanisms of nocturnal oxyhemoglobin desaturation in children and adolescents with sickle cell disease. *Pediatric Pulmonology*, *28*(6), 418–22.

Nugent, N. R., Tyrka, A. R., Carpenter, L. L., & Price, L. H. (2011). Gene-environment interactions: Early life stress and risk for depressive and anxiety disorders. *Psychopharmacology*, *214*(1), 175–196.

Ohene-frempong, B. K., Weiner, S. J., Sleeper, L. A., Miller, S. T., Embury, S., Moohr, J. W., … Gill, F. M. (1998). Cerebrovascular Accidents in Sickle Cell Disease: Rates and Risk Factors. *European Journal of Pediatrics*, *152*, 288–295.

Olley, A., Malhi, G., & Sachdev, P. (2007). Memory and executive functioning in obsessive-compulsive disorder: A selective review. *Journal of Affective Disorders*, *104*(1–3), 15–23.

Platt, O. S., Brambilla, D. J., Rosse, W. F., Milner, P. F., Castro, O., Steinberg, M. H., & Klug, P. P. (1994). Mortality in Sickle Cell Disease.*The New England Journal of Medicine,* *330*(23), 1639–1644.

Platt, O. S., Thorington, B. D., Brambilla, D. J., Milner, P. F., Rosse, W. F., Vichinsky, E., & Kinney, T. R. (2001). Pain in sickle cell disease: Rates and risk factors. *The New England Journal of Medicine*, *325*(1), 11–16.

Porter, L., Gil, K. M., Sedway, J., Ready, J., Workman, E., & Thompson, R. J. J. (1998). Pain in children and adolescents with sickle cell disease: An analysis of daily pain diaries. *International Journal of Behavioral Medicine*, *5*(3), 185–203.

Poznanski, E. O., Freeman, L. N., & Mokros, H. B. (1985). Children's Depression Rating Scale Revised. *Psychopharmacology Bulleton*, *21*, 979–989.

Prussien, K. V., Yarboi, J., Bemis, H., Williams, E., DeBaun, M., & Compas, B. E. (2016). Disease-Related Stress and Depressive Symptoms in Children with Sickle Cell Disease. In *Association for Behavioral and Cognitive Therapies*. New York, NY.

Reid, G. J., Gilbert, C. A., McGrath, P. J., Chipuer, H. M., Ellerton, M. L., & Ritchie, J. A. (1998). The pain coping questionnaire: Preliminary validation. *Pain*, *76*, 83–96.

Riggs, N. R., Blair, C. B., & Greenberg, M. T. (2003). Concurrent and 2-year longitudinal relations between executive function and the behavior of 1st and 2nd grade children. *Child Neuropsychology*, *9*(4), 267–76.

Robinson, K. E., Pearson, M. M., Cannistraci, C. J., Anderson, A. W., Kuttesch, J. F., Wymer, K., … Compas, B. E. (2014). Functional neuroimaging of working memory in survivors of childhood brain tumors and healthy children: Associations with coping and psychosocial outcomes. *Child Neuropsychology*.

Rodriguez, E. M., Dunn, M. J., Zuckerman, T., Vannatta, K., Gerhardt, C. A., & Compas, B. E. (2012). Cancer-Related Sources of Stress for Children With Cancer and Their Parents, *Journal of Pediatric Psychology, 37*(2), 185–197.

Sala, M. N., Pons, F., & Molina, P. (2014). Emotion regulation strategies in preschool children. *The British Journal of Developmental Psychology*, *32*(4), 440–53.

Sanchez, C. E., Schatz, J., & Roberts, C. W. (2010). Cerebral blood flow velocity and language functioning in pediatric sickle cell disease. *Journal of the International Neuropsychological Society*, *16*(2), 326–34.

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*(8), 1109–1111.

Schatz, J., Finke, R. L., Kellett, J. M., & Kramer, J. H. (2002). Cognitive functioning in children with sickle cell disease: a meta-analysis. *Journal of Pediatric Psychology*, *27*(8), 739–748.

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*(8), 1073–1085.

Schatz, J., Schlenz, A. M., McClellan, C. B., Puffer, E. S., Hardy, S., Pfeiffer, M., & Roberts, C. W. (2015). Changes in Coping, Pain, and Activity After Cognitive-Behavioral Training. *The Clinical Journal of Pain*, *31*(6), 536–547.

Schlenz, A. M., Schatz, J., McClellan, C. B., Sweitzer, S. M., & Roberts, C. W. (2013). Information-seeking coping behaviors during painful procedures in African-American children with sickle cell disease. *Pain Management Nursing*, *14*(3), 1–7.

Skinner, E. A., & Edge, K. (1998). Reflections on Coping and Development across the Lifespan. *International Journal of Behavioral Development*, *22*(2), 357–366.

Snyder, H. R. (2013). Major depressive disorder is associated with broad impairments on neuropsychological measures of executive function: a meta-analysis and review. *Psychological Bulletin*, *139*(1), 81–132.

Stansbury, K., & Zimmermann, L. K. (1999). Relations among child language skills, maternal socialization of emotion regulation, and child behavior problems. *Child Psychiatry and Human Development*, *30*(2), 121–142.

Steen, R. G., Fineberg-Buchner, C., Hankins, G., Weiss, L., Prifitera, A., & Mulhern, R. K. (2005). Cognitive deficits in children with sickle cell disease. *Journal of Child Neurology*, *20*(2), 102–107.

Steen, R. G., Miles, M. A., Helton, K. J., Strawn, S., Wang, W., Xiong, X., & Mulhern, R. K. (2003). Cognitive Impairment in Children with Hemoglobin SS Sickle Cell Disease: Relationship to MR Imaging Findings and Hematocrit. *American Journal of Neuroradiology*, *24*(3), 382–389.

Stegenga, K. A., Ward-Smith, P., Hinds, P. S., Routhieaux, J. A., & Woods, G. M. (2004). Quality of life among children with sickle cell disease receiving chronic transfusion therapy. *Journal of Pediatric Oncology Nursing*, *21*(4), 207–213.

Steinberg, M. H., Barton, F., Castro, O., Pegelow, C. H., Ballas, S. K., Kutlar, A., … Terrin, M. (2003). Effect of hydroxyurea on mortality and morbidity in adult sickle cell anemia: risks and benefits up to 9 years of treatment. *Journal of the American Medical Association*, *289*(13), 1645–51.

Strouse, J. J., Cox, C. S., Melhem, E. R., Lu, H., Kraut, M. A., Razumovsky, A., … Casella, J. F. (2006). Brief report Inverse correlation between cerebral blood flow measured by continuous arterial spin-labeling (CASL) MRI and neurocognitive function in children with sickle cell anemia (SCA), *108*(1), 379–382.

Thompson, R., Gil, K., & Burbach, D. (1993). Psychological adjustment of mothers of children and adolescents with sickle cell disease: The role of stress, coping methods, and family functioning. *Journal of Pediatric Psychology*, *18*(5), 549–559.

Thompson, R. J., Gustafson, K. E., Gil, K. M., Godfrey, J., & Bennett Murphy, L. M. (1998). Illness specific patterns of psychological adjustment and cognitive adaptational processes in children with cystic fibrosis and sickle cell disease. *Journal of Clinical Psychology*, *54*(1), 121–128.

Thomsen, A. H., Compas, B. E., Colletti, R. B., Stanger, C., Boyer, M. C., & Konik, B. S. (2002). Parent Reports of Coping and Stress Responses in Children With Recurrent Abdominal Pain. *Journal of Pediatric Psychology*, *27*(3), 215–226.

Thornburg, C. D., Calatroni, A., & Panepinto, J. A. (2011). Differences in Health-Related Quality of Life in Children With Sickle Cell Disease Receiving Hydroxyurea. *Journal of Pediatric Hematology and Oncology*, *33*(4), 251–254.

Trzepacz, A. M., Vannatta, K., Gerhardt, C. A., Ramey, C., & Noll, R. B. (2004). Emotional, social, and behavioral functioning of children with sickle cell disease and comparison peers. *Journal of Pediatric Hematology and Oncology*, *26*(10), 642–648.

Tsunoka, T., Kishi, T., Ikeda, M., Kitajima, T., Yamanouchi, Y., Kinoshita, Y., … Iwata, N. (2009). Association analysis of Group II metabotropic glutamate receptor genes (GRM2 and GRM3) with mood disorders and fluvoxamine response in a Japanese population. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, *33*(5), 875–879.

Wadsworth, M. E., Rieckmann, T., Benson, M. A., & Compas, B. E. (2004). Coping and responses to stress in Navajo adolescents: Psychometric properties of the responses to stress questionnaire. *Journal of Community Psychology*, *32*(4), 391–411.

Walker, L. S., Garber, J., Smith, C. a, Van Slyke, D. a, & Claar, R. L. (2001). The relation of daily stressors to somatic and emotional symptoms in children with and without recurrent abdominal pain. *Journal of Consulting and Clinical Psychology*, *69*(1), 85–91.

Watkins, K. E., Hewes, D. K., Connelly, A., Kendall, B. E., Kingsley, D. P., Evans, J. E., … Kirkham, F. J. (1998). Cognitive deficits associated with frontal-lobe infarction in children with sickle cell disease. *Developmental Medicine and Child Neurology*, *40*(8), 536–43.

Wechsler, D. (1991). *The Wechsler intelligence scale for children--third edition.* San Antonio, TX: The Psychological Corporation.

Wechsler, D. (2003). *Wechsler intelligence scale for children--fourth edition.* San Antonio, TX: Pearson.

Wechsler, D. (2011). *Wechsler abbreviated scale of intelligence, second edition manual.* Bloomington, MN: Pearson.

Willcutt, E. G., Doyle, A. E., Nigg, J. T., Faraone, S. V., & Pennington, B. F. (2005). Validity of the executive function theory of attention- deficit/hyperactivity disorder: A meta-analytic review. *Biological Psychiatry*, *57*, 1336–1346.

Yang, Y. M., Cepeda, M., Price, C., Shah, A., & Mankad, V. (1994). Depression in children and adolescents with sickle cell disease. *Archives of Pediatric and Adolescent Medicine*, *148*, 457–460.

Yao, S., Xiao, J., Zhu, X., Zhang, C., Auerbach, R. P., McWhinnie, C. M., … Wang, C. (2010). Coping and involuntary responses to stress in Chinese university students: psychometric properties of the responses to stress questionnaire. *Journal of Personality Assessment*, *92*(4), 356–361.

Yarboi, J., Compas, B. E., Brody, G. H., White, D., Rees Patterson, J., Ziara, K., & King, A.

(2015). Association of social-environmental factors with cognitive function in children with sickle cell disease. *Child Neuropsychology, 7049*, 1–18.

TABLES

Table 1. *Demographics of Children with SCD and Their Primary Caregiver*

	Caregiver	Child
Age, *M* (*SD*)	39.57 (9.43)	9.30 (3.03)
Sex, *n* (%)		
Female	35 (79.5)	20 (42.6)
Male	9 (20.5)	27 (57.4)
Race/ethnicity, *n* (%)		
Black/African American	42 (95.5)	43 (91.5)
Other	2 (4.5)	1 (2.1)
Main caregiver, *n* (%)		
Biological parent	30 (68.2)	
Biological father	8 (18.2)	
Adoptive parent	1 (2.3)	
Grandparent	3 (6.8)	
Other	2 (4.5)	
Parent education, *n* (%)		
Below high school	4 (9.1)	
High school graduate	10 (22.7)	
Some college	17 (38.6)	
College degree	12 (27.3)	
Household income, *n* (%)		
\$25,000 or under	16 (36.4)	
\$25,001 – \$50,000	13 (29.5)	
\$50,001 – \$75,000	7 (15.9)	
\$75,001 – \$100,000	4 (9.1)	
\$100,000 or more	3 (6.8)	
Medical characteristics		
Type of SCD, *n* (%)		
HbSS		32 (68.1)
HbSC		9 (19.1)
HBβ-Thalaseemia		5 (10.6)
Hgb at clinic appointment, *M* (*SD*)		9.7 (1.6)
WBC at clinic appointment, *M* (*SD*)		9.5 (3.3)
History of overt stroke, *n* (%)		3 (6.4)
History of silent stroke, *n* (%)		7 (14.9)

Table 2. *Means and Standard Deviations for Measures of Children's Cognitive Functioning, Emotional Distress, and Coping*

Variables	*M*	*SD*	*t*
Cognitive function domain			
Working memory	93.09	14.11	-3.36^{**}
Verbal comprehension	93.34	11.74	-3.89^{***}
Emotional distress			
Anxiety symptoms	53.74	6.23	3.94^{***}
Depressive symptoms	55.95	7.93	4.93^{***}
Anxious-Depressed	53.42	7.13	3.15^{**}
	Parent/self		
Child coping			
Primary control	0.19/0.19	0.03/0.04	
Secondary control	0.27/0.26	0.06/0.04	
Disengagement	0.14/0.16	0.03/0.03	

Scores for working memory and verbal comprehension are standardized (*M* = 100, *SD* = 15), and scores for the CBCL are standardize T-scores (*M* = 50, *SD* = 10).

Table 3. *Correlations Among Cognitive Function, Emotional Distress, and Parent Report of Child Coping*

	1	2	3	4	5	6	7
1. Working memory	-						
2. Verbal comprehension	.57**	-					
3. Anxiety symptoms	-.23	-.06	-				
4. Depressive symptoms	-.38*	-.14	.71**	-			
5. Anxious-depressed	-.14	.09	.79**	.81**	-		
6. Primary control	.08	-.07	-.17	-.20	-.34*	-	
7. Secondary control	.14	.42**	-.27^{+}	-.35*	-.13	-.01	-
8. Disengagement	-.07	-.18	.17	.18	.12	-.41**	-.52**

$^{+}p<.10$; $^{*}p<.05$; $^{**}p<.01$

Table 4. *Summary of Linear Multiple Regression Analyses Predicting Parent Report of Child Secondary Control Coping*

	B	β	*t*
Step 1: $R^2 = .06$			
Working memory	.00	.10	.57
Diagnosis	-.02	-.19	-.84
Hgb at clinic appointment	.00	.08	.34
History of stroke	-.03	-.20	-1.12
Step 2: $R^2 = .24$			
Working memory	-.00	-.21	-1.11
Verbal comprehension	.00	.51	2.89^{**}
Diagnosis	-.01	-.16	-.73
Hgb at clinic appointment	.00	.05	.24
History of stroke	-.03	-.23	-1.45

$^{**}p<.01$

Table 5. *Summary of Linear Multiple Regression Analyses of Child Cognitive Functioning Predicting Parent Report of Depressive Symptoms*

	B	β	*t*
Step 1: $R^2 = .18$			
Working memory	-.23	-.42	-2.65^*
Diagnosis	1.93	.17	.78
Hgb at Clinic Appointment	-.63	-.13	-.62
History of Stroke	-2.06	-.11	-.66
Step 2: $R^2 = .19$			
Working memory	-.27	-.51	-2.63^*
Verbal comprehension	.10	.15	.81
Diagnosis	2.06	.18	.83
Hgb at clinic appointment	-.67	-.14	-.65
History of stroke	-2.27	-.12	-.72

$^*p<.05$

Table 6. *Summary of Linear Multiple Regression Analyses of Parent Report of Child Coping Predicting Parent Report of Child Depressive Symptoms*

	B	β	*t*
Step 1: $R^2 = .16$			
Secondary control coping	-41.23	-.36	-2.23^{*}
Diagnosis	1.60	.15	.64
Hgb at clinic appointment	-.94	-.22	-1.00
History of Stroke	-.02	-.00	-.01
Step 2: $R^2 = .21$			
Secondary control coping	-44.78	-.39	-1.95^{+}
Primary control coping	-53.69	-.25	-1.34
Disengagement	-12.65	-.05	-.21
Diagnosis	2.10	.19	.82
Hgb at clinic appointment	-.92	-.21	-.93
History of stroke	-.31	.02	-.11

$^{+}p<.10$; $^{*}p<.05$

FIGURES

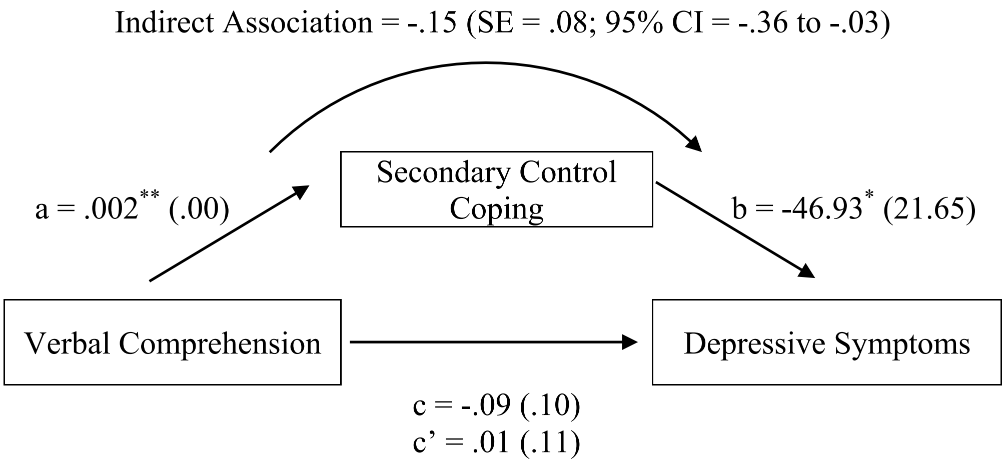

Figure I. Direct and indirect associations of verbal comprehension with depressive symptoms through secondary control coping. Unstandardized path coefficients with standard errors in parentheses.
$^{*}p<.05$; $^{**}p<.01$

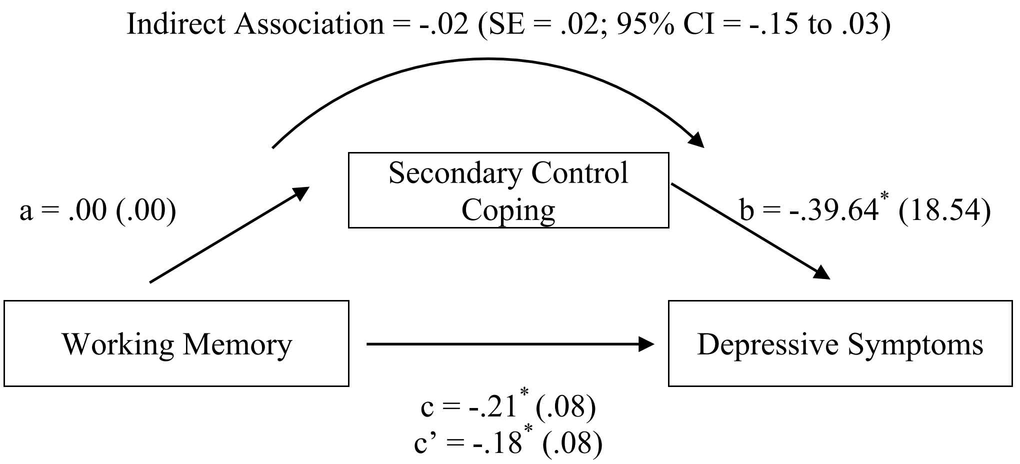

Figure II. Direct and indirect associations of working memory with depressive symptoms through secondary control coping. Unstandardized path coefficients with standard errors in parentheses.
$^{*}p<.05$; $^{**}p<.01$