

# Cognitive Function, Coping, and Depressive Symptoms in Children and Adolescents with Sickle Cell Disease

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Received June 28, 2017; revisions received October 30, 2017; accepted October 31, 2017

## Abstract

**Objective** The objective of this study was to investigate the association between cognitive functioning, coping, and depressive symptoms in children and adolescents with sickle cell disease (SCD).

**Method** Forty-four children ( $M$  age = 9.30,  $SD$  = 3.08; 56.8% male) with SCD completed cognitive assessments measuring working memory (Wechsler Intelligence Scale for Children-Fourth Edition) and verbal comprehension (Wechsler Abbreviated Scale of Intelligence-Second Edition). Participants' primary caregivers completed questionnaires assessing their child's coping and depressive symptoms. **Results** Verbal comprehension was significantly positively associated with secondary control coping (cognitive reappraisal, acceptance, distraction), and both working memory and secondary control coping were negatively associated with depressive symptoms. In partial support of the primary study hypothesis, verbal comprehension had an indirect association with depressive symptoms through secondary control coping, whereas working memory had a direct association with depressive symptoms. **Conclusions** The results provide new evidence for the associations between cognitive function and coping, and the association of both of these processes with depressive symptoms in children with SCD. Findings provide potential implications for clinical practice, including interventions to improve children's cognitive functioning to attenuate depressive symptoms.

**Key words:** children; cognitive assessment; coping; depressive symptoms; sickle cell disease.

Sickle cell disease (SCD) is composed of a group of disorders characterized by abnormal hemoglobin (HbS) that primarily occur in one in every 400 African American newborns in the United States (Hassell, 2010; Lorey, Arnopp, & Cunningham, 1996). It is associated with medical difficulties such as chronic anemia, recurrent pain episodes, and cerebral infarcts including observable and silent strokes. These medical difficulties are accompanied by a number of negative sequelae of the disease including problems in neurocognitive functioning. Children with SCD with and

without a history of cerebral infarct show significant deficits in Full Scale IQ, verbal reasoning, and executive function relative to healthy controls and national norms (Berg, Edwards, & King, 2012; Hensler et al., 2014; King et al., 2014; Schatz et al., 2002; Schatz & Roberts, 2005; Yarboi et al., 2017).

Deficits in verbal and executive function skills may have far-reaching effects, including increased risk for depressive symptoms. A meta-analysis by Snyder (2013) found a reliable association between cognitive function and depression in diverse samples (e.g., children,

adolescents, adults) without a coexisting medical condition, such that lower scores on measures of executive function and verbal fluency were related to more severe symptoms of depression, with a medium and small effect, respectively. Prior research has found similar associations in pediatric populations (e.g., brain tumors, [Robinson et al., 2015](#)); however, the association between cognitive problems in children with SCD and depressive symptoms remains unknown.

Findings regarding depression in children with SCD have been mixed ([Benton, Ifeagwu, & Smith-Whitley, 2007](#)); however, several studies show that they are at risk for experiencing internalizing symptoms, including symptoms of anxiety and depression ([Benton et al., 2011](#)), and are more likely to exceed clinical cut-offs compared with their healthy peers ([Trzepacz, Vannatta, Gerhardt, Ramey, & Noll, 2004](#)). Given the evidence of depressive symptoms in adults with SCD ([Jonassaint, Jones, Leong, & Frierson, 2016](#)) and the association between deficits in domains of cognitive function and depression, further examination of these symptoms and their correlates during childhood and adolescence is warranted.

In addition to problems in cognitive function, exposure to chronic disease-related stress and other sources of stress is another potentially important risk factor for symptoms of depression in children with SCD. While research in this population has focused on pain-related stress ([Mitchell et al., 2007](#)), other disease-related stressors such as disruptions in daily role functioning, social challenges, and treatment and side effects are also significant sources of stress for this population ([Hildenbrand, Barakat, Alderfer, & Marsac, 2013](#)). Studies of other pediatric populations (e.g., cancer) show that disease and treatment-related stressors are related to symptoms of distress ([Rodriguez et al., 2012](#)), suggesting that it may be important to examine how children with SCD cope with a range of disease-related stressors.

Given the findings of the association between stress and depressive symptoms in children with SCD, the ways that these children cope with stress may also be important to examine. While children in this population may be faced with other significant stressors (e.g., socioeconomic-related stressors; [Yarboi et al., 2017](#)), we will focus on how they cope with SCD-specific stress to capture the situation-specific nature of coping and emotion regulation. Previous research in children with SCD has been guided primarily by the model of pain coping by [Gil, Williams, Thompson, and Kinney \(1991\)](#), composed of active coping attempts, negative thinking, and passive adherence. Pain coping attempts are associated with the experience and management of pain, daily functioning, and health-care utilization ([Gil et al., 1997](#); [Gil et al., 2001](#); [Mitchell et al., 2007](#);

[Schatz et al., 2015](#)). Studies reveal a positive association between negative thinking and symptoms of depression, inconsistent findings for passive adherence, and no associations for active coping attempts ([Barakat, Schwartz, Simon, & Radcliffe, 2007](#); [Gil et al., 1991](#)); however, only these limited studies have examined the association between coping and emotional distress.

An alternative framework for understanding coping is organized around the actual and perceived controllability of a stressor ([Compas et al., 2012, 2017](#)). Chronic illness in children, including SCD, presents a wide range of uncontrollable stressors. In comparison with the pain coping model, a control-based model of coping and emotion regulation organizes engagement coping into three distinct groups: primary control coping, secondary control coping, and disengagement ([Compas et al., 2012, 2017](#)). Primary control coping includes 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, emotional modulation). Secondary control coping reflects efforts to adapt to the demands of a stressor and includes cognitive reappraisal, positive thinking, acceptance, and distraction. Finally, disengagement involves direct attempts to orient oneself away from the stressor (e.g., avoidance, wishful thinking, denial). While this model has yet to be examined in children with SCD, studies of children coping with cancer and recurrent abdominal pain found that children's use of secondary control coping accounted for unique variance in symptoms of depression ([Compas et al., 2006, 2014](#)).

Cognitive abilities, including executive function, may serve as a significant resource for adaptive coping and emotion regulation ([Allen, Anderson, Rothman, & Bonner, 2016](#); [Hocking et al., 2011](#); [Robinson et al., 2015](#)). For example, secondary control coping strategies may rely on working memory, which includes the ability to hold information in short-term memory and view it from an alternative perspective. In a sample of children with leukemia, [Campbell et al. \(2009\)](#) found that executive function was positively associated with the use of secondary control coping, and coping partially accounted for the association between executive function and internalizing symptoms. Children's verbal skills are also associated with coping and emotion regulation, including greater use of seeking social support, cognitive reappraisal, and distraction in stressful situations ([Sala, Pons, & Molina, 2014](#)). Verbal abilities 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](#)). These cognitive processes may be important for children with chronic illnesses because their ability to cope with

stress may be compromised by deficits in executive functioning and verbal comprehension as a result of the illness or its treatment (Compas, Jaser, Reeslund, Patel, & Yarboi, 2017).

No study has examined the associations among cognitive function, coping, and emotional distress in children and adolescents with SCD, and the control-based model of coping has yet to be assessed in this population. The purpose of the present study was to address these gaps in the literature and to test direct and indirect associations between cognitive functioning and depressive symptoms through coping. The following preliminary hypotheses were tested: (1) Working memory and verbal comprehension will be positively associated with secondary control coping. (2) Working memory and verbal comprehension will be negatively associated with depressive symptoms. (3) Based on research in other pediatric populations (Compas et al., 2012), secondary control coping, but not primary control coping or disengagement coping, will be negatively related to depressive symptoms. Finally, the primary hypothesis of this study was that (4) secondary control coping will account for a significant portion of the variance in the association between cognitive functioning and depressive symptoms. Given that deficits in cognitive functioning increase with age, a history of stroke, and disease severity (King et al., 2014; Schatz et al., 2002), these variables were used as covariates.

## Method

### Participants

Participants included 44 children and adolescents with SCD ages 6 to 16 years (mean [ $M$ ] = 9.30, standard deviation [ $SD$ ] = 3.08), 56.8% male. Participants represented a variety of SCD subtypes: 70.5% were diagnosed with HbSS, 20.5% were diagnosed with HbSC, and 9.1% with variations of S-beta thalassemia. Results from patients' most recent MRI scans indicated that the majority of children (35; 77.3%) displayed no evidence of cerebral infarct. Of the remaining 22.7%, six patients had a history of silent stroke, two with a history of overt stroke, and one with both silent and overt stroke. Children did not differ on cognitive scores, coping ratio scores, or depressive symptoms based on SCD subtypes, history of stroke, or gender. Twenty-nine participants (65.9%) were treated with hydroxyurea and six (13.6%) had a current chronic transfusion plan, all of whom had a history of stroke. Participants had an average hemoglobin level of 9.69 ( $SD$  = 1.57, range = 6.6 to 13.4) at the clinic appointment closest to the study visit ( $M$  = 52.28 days). The majority of the sample (97.7%) identified as African American. Nearly 7% of the sample 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), but also included adoptive parents ( $n$  = 1), grandparents ( $n$  = 3), and other primary caregivers ( $n$  = 2). Caregivers ranged in age from 25 to 60 years ( $M$  = 39.57,  $SD$  = 9.43), and 79.5% were female. Only one caregiver reported her own diagnosis of SCD. Caregivers came from a range of educational background (11th grade to 3 years of graduate school;  $M$  = 13.65 years of education) as well as annual family income levels (37.2% earned  $\leq$ \$25,000; 30.2% earned \$25,001–\$50,000; 16.3% earned \$50,001–\$75,000; 9.3% earned \$75,001–100,000; and 7.0% earned  $\geq$ \$100,000).

### Procedure

Families were recruited to participate in a study of stress, parenting, and cognitive function in children with SCD and their parents between 2013 and 2016. Eligibility requirements included (a) confirmed diagnosis of SCD in the child, (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 (however, no children in the current sample were excluded for these reasons). Informed consent and assent were obtained from caregivers and children, respectively, before study entry and participation. The study protocol was reviewed and approved by the Vanderbilt University institutional review board.

Recruitment occurred at a university-based children's hospital and an affiliated community clinic in the southeastern United States where participants received their care. Eligible families were identified by members of the pediatric hematology medical team, and during routine appointments, 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 office-based laboratory visit, children completed a brief cognitive assessment battery. Caregivers also completed a series of questionnaires assessing family sociodemographics, child coping, and child distress. Families received compensation at the end of the visit and were reimbursed for travel.

### Measures

#### Demographic and Medical Data

Parents provided demographic information, including age, education level, race, family income, and marital status. Parents gave permission to the research staff to

access their child's medical charts, where the child's hemoglobin level at the clinic visit closest to the study visit and stroke status were extracted.

### Working Memory

Children were administered the Working Memory Index (WMI) from the Wechsler Intelligence Scale for Children-Fourth Edition (Wechsler, 2003). The WMI, composed of the Digit Span and Letter-Number Sequencing subtests, is a measure of the ability to sustain attention and exert mental control with auditory stimuli.

### Verbal Comprehension

Children completed the Vocabulary and Similarities subtests of the Wechsler Abbreviated Scale of Intelligence-Second Edition (WASI-II; Wechsler, 2011). The WASI-II is widely used as a brief measure of intelligence in children and adults. The Verbal Comprehension Index (VCI) is composed of the Vocabulary and Similarities subtests and is designed to measure verbal skills. In the current sample, the correlation between the WMI and VCI was  $r = .57$ ,  $p < .001$ . The Wechsler scales have been shown to be valid and reliable measures of cognitive functioning in children (Sattler, 2008).

### Coping

The Responses to Stress Questionnaire-Sickle Cell Disease version (RSQ-SC; Connor-Smith et al., 2000) was used to obtain parent-reported child coping. The RSQ-SC version includes a list of eight 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 stressors. Because this study was focused on children's coping responses, only the three voluntary coping scales are reported: 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 (Connor-Smith et al., 2000).

Internal consistencies for parent reports of child coping are as follows: 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 (e.g., Native American, Chinese,

Spanish, Bosnian) coping with a variety of stressors (Benson et al., 2011; Compas et al., 2006; Yao et al., 2010); however, the current study is the first to use this instrument with children and adolescents with SCD. Studies in children with cancer show that parent reports and self-reports of child coping are significantly correlated with a medium effect (Compas et al., 2014).

### Depressive Symptoms

Child symptoms of depression were assessed using caregiver report on the Child Behavior Checklist (CBCL; Achenbach & Rescorla, 2001). Reliability and validity are established for the CBCL, and normative  $T$  scores are derived from parents' report on a nationally representative sample of children aged 6 to 17 years. Depressive symptoms were measured with the Affective Problems DSM-oriented scale; items include, "there is very little he/she enjoys," "cries a lot," "feels worthless or inferior." This scale has often been used to measure depressive symptoms in children with chronic illnesses (Pinquart & Shen, 2011). One participant was identified as an outlier on the Affective Problems scale ( $T = 76$ ) and was excluded from analyses. Internal consistency for this scale was  $\alpha = .78$ .

### Statistical Analyses

Working memory and verbal comprehension scores were compared with normative data using independent sample  $t$ -tests. Power analysis indicated that with  $n = 43$ ,  $\beta = .80$ , and  $\alpha = .05$ , two-tailed, significant correlations of medium-to-large effect sizes ( $r \geq .41$ ) could be detected. Pearson correlations were performed to determine significant bivariate associations between cognitive function, coping, and distress using SPSS (24th edition). To evaluate indirect associations between cognitive function and depressive symptoms accounted for by secondary control 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 the total direct (path  $c$ ,  $c'$ ) and indirect (path  $ab$ ) effects, described with unstandardized regression coefficients. The current analyses were conducted with a 95% confidence interval for the indirect effect with 10,000 bootstrap samples. An indirect effect contributes significantly to the model when the confidence interval of the indirect path does not contain zero (Hayes, 2009). Similar analyses have been used with other pediatric and child samples in prospective and cross-sectional designs (Murphy et al., 2015; Okonofua & Eberhardt, 2015). Covariates (SCD type, clinic hemoglobin, history of stroke, and age) were added in



**Table I.** Descriptive Statistics for Measures of Children's Cognitive Function, Emotional Distress, and Coping

|                           | Range     | M     | SD    |
|---------------------------|-----------|-------|-------|
| Cognitive function domain |           |       |       |
| Working memory            | 62–116    | 92.39 | 13.90 |
| Verbal comprehension      | 62–123    | 93.39 | 12.08 |
| Emotional distress        |           |       |       |
| Depressive symptoms       | 50–76     | 55.95 | 7.93  |
| Child coping              |           |       |       |
| Primary control           | 0.12–0.26 | 0.19  | 0.03  |
| Secondary control         | 0.18–0.40 | 0.27  | 0.06  |
| Disengagement             | 0.09–0.10 | 0.14  | 0.02  |

\*\* $p < .01$ ; \*\*\* $p < .001$ . Scores for Wechsler Intelligence Scale for Children-Fourth Edition Working Memory Index and Wechsler Abbreviated Scale of Intelligence-Second Edition Verbal Comprehension Index are standardized ( $M = 100$ ,  $SD = 15$ ), and scores for the CBCL Affective Problems DSM-oriented scale measuring depressive symptoms are standardized  $T$ -scores ( $M = 50$ ,  $SD = 10$ ). Responses to Stress Questionnaire-Sickle Cell Disease version-measured coping is reported in ratio scores;  $n = 44$ .

secondary analyses, and age was tested as a moderator of the indirect associations.

## Results

### Descriptive Statistics

Variable ranges, means, and standard deviations are reported in Table I. Children obtained a mean score of 93.9 ( $SD = 14.11$ ) on the WMI and a mean score of 93.34 ( $SD = 11.74$ ) on the VCI. Reports of child CBCL Affective Problems ( $M = 55.95$ ,  $SD = 7.93$ ) showed a medium effect for elevated depressive symptoms compared with norms,  $t(42) = 4.93$ ,  $p < .001$ ,  $d = 0.66$ .

*Hypothesis 1: WMI and VCI will be positively associated with secondary control coping.*

Bivariate Pearson correlations showed that the WMI was not related to secondary control coping ( $r = .15$ ,  $p = .338$ ). The VCI, however, was positively and significantly related to secondary control coping ( $r = .43$ ,  $p = .004$ ). Neither WMI nor VCI was related to primary control coping (WMI:  $r = .09$ ,  $p = .559$ ; VCI:  $r = -.04$ ,  $p = .811$ ) or disengagement (WMI:  $r = -.08$ ,  $p = .627$ ; VCI:  $r = -.20$ ,  $p = .205$ ). Bonferroni correction for familywise error reduced  $p < .008$ , meaning the significant association between VCI and secondary control remained.

*Hypothesis 2: WMI and VCI will be negatively associated with depressive symptoms.*

WMI was significantly and negatively associated with depressive symptoms ( $r = -.38$ ,  $p = .012$ ). The VCI was not related to symptoms ( $r = -.14$ ,  $p = .395$ ). After correcting for familywise error ( $p < .025$ ), the association between WMI and symptoms remained significant.

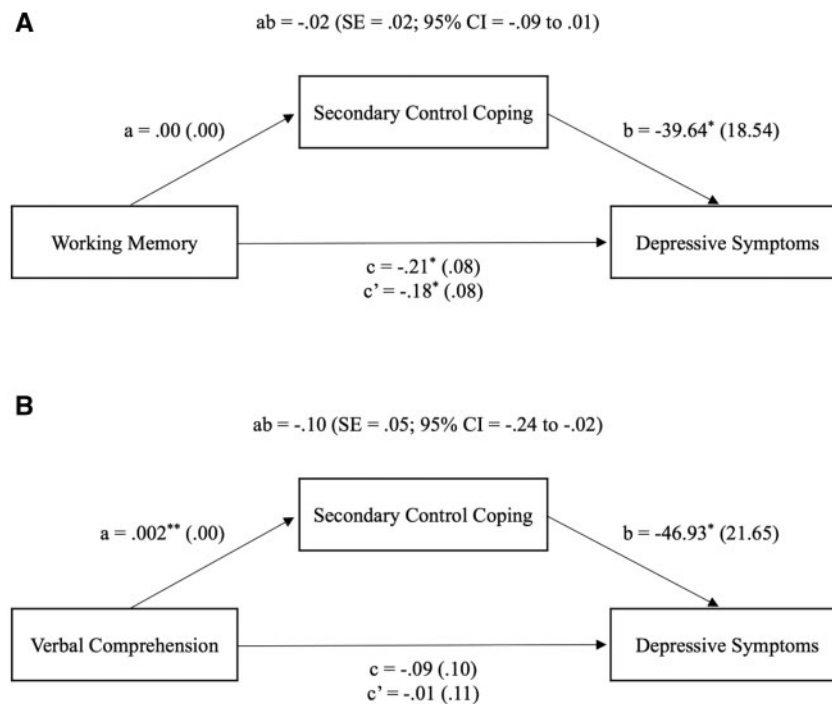
*Hypothesis 3: Secondary control coping will be negatively associated with depressive symptoms.*

Secondary control coping was significantly and negatively associated with depressive symptoms ( $r = -.35$ ,  $p = .022$ ). Neither primary control coping ( $r = -.20$ ,  $p > .20$ ) nor disengagement coping ( $r = .18$ ,  $p > .20$ ) was significantly related to symptoms. After correcting for familywise error ( $p < .008$ ), no correlations between coping and symptoms were significant.

*Hypothesis 4: Secondary control coping will account for a significant portion of the variance in the association between domains of cognitive functioning and depressive symptoms.*

The direct and indirect paths for the association between the WMI and depressive symptoms through coping are shown in Figure 1A. There was no association between the WMI and secondary control coping (path  $a = .00$ ,  $p = .362$ ), but secondary control coping was significantly related to depressive symptoms (path  $b = -.39.64$ ,  $p = .039$ ). Although there was not an indirect association through coping (path  $ab = -.02$ , Boot SE = .02, 95% CI =  $-.09$  to  $.01$ ), there was a direct association between the WMI and symptoms (path  $c = -.21$ ,  $p = .012$ ; path  $c' = -.18$ ,  $p = .021$ ). The same pattern of significant paths was found when SCD type, hemoglobin, history of stroke, and age were included as covariates (path  $a = .00$ ,  $p = .709$ ; path  $b = -.38.60$ ,  $p = .046$ ; path  $c = -.18$ ,  $p = .044$ ; path  $c' = -.17$ ,  $p = .049$ ; path  $ab = -.01$ , Boot SE = .02, 95% CI =  $-.07$  to  $.03$ ). Age approached significance in predicting symptoms when coping was included in the model with the other covariates ( $B = .69$ ,  $p = .070$ ) and when it was not ( $B = .77$ ,  $p = .055$ ).

Figure 1B shows coefficients for the direct and indirect associations between the VCI and depressive symptoms through coping. Consistent with bivariate analyses, there was a significant path coefficient from the VCI to secondary control coping (path  $a = .002$ ,  $p = .006$ ), and coping was also related to depressive symptoms (path  $b = -.46.93$ ,  $p = .036$ ). There was not a direct association between the VCI and symptoms, shown by path  $c (-.09$ ,  $p = .395$ ) and path  $c' (.01$ ,  $p = .925$ ) in Figure 1B. The analysis showed that there was a significant indirect association, such that secondary control coping accounted for a significant portion of the variance in the association between the VCI and depressive symptoms (path  $ab = -.10$ , Boot SE = .05, 95% CI =  $-.24$  to  $-.02$ ). A similar pattern of significant associations was found when this model controlled for SCD type, hemoglobin level at clinic, history of stroke, and age (path  $a = .00$ ,  $p = .011$ ; path  $b = -.41.71$ ,  $p = .062$ ; path  $c = -.07$ ,  $p = .459$ ; path  $c' = -.01$ ,  $p = .935$ ; path  $ab = -.08$ , Boot SE = .05, 95% CI =  $-.23$  to  $-.01$ ). Age was a significant predictor when secondary control coping was in the model ( $B = .98$ ,  $p = .016$ ) and when it was not ( $B = .90$ ,  $p = .023$ ).



**Figure 1.** (A) Direct and indirect associations of working memory with depressive symptoms through secondary control coping without covariates. (B) Direct and indirect associations of verbal comprehension with depressive symptoms through secondary control coping without covariates. Unstandardized path coefficients with standard errors are given in parentheses. The PROCESS macro program only produces unstandardized regression coefficients. Owing to the difference in scaling between the standard scores on the VCI and the ratio scores from the Responses to Stress Questionnaire-Sickle Cell Disease version, the unstandardized path coefficient is small.

\* $p < .05$ ; \*\* $p < .01$ . ( $n = 43$ )

Using PROCESS macro Model 14, we conducted supplemental analyses to assess child age as a potential moderator of the indirect association between the domains of cognitive function and depressive symptoms. There was a significant conditional indirect association between the VCI and depressive symptoms at the mean age and 1 SD above the mean, but the indirect association was not significant 1 SD below the mean; nevertheless, there was not a significant difference in the conditional indirect effects. There were no significant conditional indirect association of WMI on depressive symptoms at any age level.

## Discussion

Children and adolescents with SCD are faced with significant stress related to their disease and its management. Although there are other environmental stressors that could influence depressive symptoms, this study assessed how children with SCD coped with stress specifically related to their illness. Understanding how children cope with SCD-related stress, including but not limited to pain, and the impact of cognitive function on adjustment may be important to inform interventions for this population. The current study draws on a control-based model of

coping, and it provides evidence for the direct association of working memory and secondary control coping with depressive symptoms, as well as an indirect association of verbal comprehension with symptoms through coping in children with SCD.

Levels of depressive symptoms in this sample suggest that children with SCD experience moderate depressive symptoms, comparable with findings in previous studies (Thompson et al., 1998; Trzepacz et al., 2004). Prior research on increased risk for depressive symptoms in African American youth has been inconsistent (Taylor et al., 2014), suggesting elevated symptoms may be attributable to SCD-related stress. However, it is noteworthy that some symptoms of internalizing problems may be confounded with symptoms of the child's illness and the side effects of treatment (Drotar, Stein, & Perrin, 1995); nevertheless, children with SCD may still be at increased risk for other symptoms of depression.

In partial support of the first hypothesis, our findings demonstrate that verbal comprehension was positively associated with secondary control coping, whereas working memory was not. Further, results showed that even when controlling for age and medical characteristics, verbal comprehension remained a significant predictor of secondary control coping. This

finding is consistent with the previous literature on verbal skills and emotion regulation (Sala, Pons, & Molina, 2014) and supports the hypothesis that verbal skills may play a role in emotion regulation and coping strategies, particularly in relation to cognitive reappraisal, which relies heavily on internal self-speech. Thus, impairment in verbal comprehension in children with SCD may influence how they are able to cope with stress related to the disease.

The second hypothesis, that cognitive function would be significantly related to distress, was also partially supported. Working memory was related to depressive symptoms, whereas verbal comprehension was not, even when controlling for medical characteristics and age. 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 (Snyder, 2013).

In support of the third hypothesis, secondary control coping was significantly associated with depressive symptoms even when controlling for medical characteristics associated with disease severity (disease subtype, hemoglobin level, history of stroke). This current study was the first to assess a control-based model of coping in a sample of children with SCD. The use of reappraisal, acceptance, and distraction to cope with disease-related stress was significantly related to fewer depressive symptoms. The association between secondary control coping and internalizing symptoms has been shown in previous studies of children with cancer and recurrent abdominal pain (Compas et al., 2014; Compas et al., 2006; Thomsen et al., 2002). Further, as expected, neither primary control coping nor disengagement showed significant associations with symptoms. Previous research using the Gil et al. (1991) model of pain coping has only found associations between a subtype of coping labeled negative thinking and higher levels of distress in children with SCD. As many of the disease-related stressors experienced by pediatric SCD patients are beyond their control, the control-based model of coping may capture the process of coping with regard to its association with depressive symptoms better than the pain coping model. Specifically, there may be a fit between the use of secondary control coping (e.g., acceptance, cognitive reappraisal) and the experience of uncontrollable stress in children with SCD (Compas et al., 2012).

Finally, the fourth and primary 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 association with these symptoms through secondary control coping. These findings have two important implications. First, cognitive

impairment in children with SCD, which occurs as a function of the illness itself and other environmental factors, is related to depressive symptoms within this sample. Second, how a child copes with the stressors associated with SCD is important in the association between cognitive functioning and depressive symptoms. Previous studies have found both a direct and indirect association for executive function in children with leukemia (Campbell et al., 2009) and brain tumors (Robinson et al., 2015); however, no study has looked at how verbal comprehension could be associated with depressive symptoms in pediatric and other child populations.

The current study had several strengths, including the use of a multimethod approach including direct assessment of cognitive function, nationally normed measures of depressive symptoms, and parent-reported questionnaires in a sample of children with SCD receiving the most up-to-date medical treatments. However, it is important to address the limitations of this study in future research. First, because the study was cross-sectional, temporal precedence among the variables was not established and true mediation could not be tested. Future work will benefit from a longitudinal design to determine how cognitive function, coping, and depressive symptoms are related across time. Second, owing to age restrictions on measures, only parent reports of child coping and emotional distress were examined, increasing shared variance. Future research must include both parent and adolescent self-reports of coping and distress, and alternative methods could be used to assess these constructs within younger children. Third, there was relatively low statistical power that could only identify medium to large effects. While we maintained most of our bivariate findings after correction for Type I error, a larger sample size in future research will allow for more sensitive tests of moderator effects of cognition on coping and distress. Finally, the sample was heterogeneous in age, sociodemographic characteristics, treatment type, and disease subtype. Although many of these factors were added as covariates within the analyses, future research would benefit from investigating a more homogenous high-risk sample of children with SCD (e.g., adolescents, low SES, HbSS).

The results of this study show that deficits in verbal comprehension are associated with how children cope with the stress of the illness, and both working memory and verbal reasoning are related to their emotional well-being. Depressive symptoms could be assessed regularly during medical appointments. The timing of the measures collected here were arbitrary, suggesting that the moderate level of symptoms may be a general baseline for this population. Findings suggest two specific targets for intervention research: improving executive functioning and working memory may have a

direct effect on depressive symptoms or vice versa. Clinical intervention may benefit from targeting coping to increase secondary control coping; however, the ability to effectively teach these cognitively complex coping skills may be limited by the cognitive abilities of the child. Verbal and written material on coping and emotion regulation should be matched to the cognitive level of the patient, and if possible, cognitive remediation and training in verbal and executive functioning should accompany psychosocial intervention.

### Acknowledgments

The authors are grateful to Maureen Sanger, Shannon Radomski, Mary Paty Bryant, Olivia Knoll, Caitlyn Ko, Radha Sathanayagam, and Lauren Henry for their contributions to the study.

### Funding

This work was supported by the Eunice Kennedy Shriver National Institute of Child Health and Human Development (R21HD075005) and a training grant from the National Institute of Mental Health (T32-MH18921).

*Conflicts of interest:* None declared.

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