The Association of Social-Environmental Factors with Cognitive Function in Children with Sickle Cell Disease

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ABSTRACT

Sickle cell disease is a chronic, life-threatening condition that affects more than one in every 400 African-American newborns. In addition to being at greater risk for cognitive impairment, children with sickle cell disease are also more likely to come from low-income, chaotic homes. The present study examined the relationship between cognitive function in pediatric sickle cell disease patients and their mothers' reports of social-environmental stress, psychological distress, and parenting. Sixty-five children with sickle cell disease completed a comprehensive neuropsychological testing battery while their mothers completed questionnaires included in a parent interview at baseline and at follow-up 12-24 months later. The results showed partial support for the hypothesis that greater maternal social-environmental stress and psychological distress and less positive parenting would be associated with poorer cognitive function in children with sickle cell disease. Additionally, a series of linear regression analyses showed that maternal financial stress was the strongest and most consistent predictor across all domains of cognitive function. The rationale and implications of these findings are discussed.

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CHAPTER I

INTRODUCTION

Sickle cell disease (SCD) is a chronic, life-threatening condition that affects more than one in every 400 African-American newborns. In addition to a number of debilitating physical complications, patients with SCD are also at an increased risk for considerable cognitive impairment. As screening and treatment options improve and greater numbers of pediatric SCD patients are surviving into adulthood, there is an increased interest in identifying the underlying causes of these marked decrements in cognitive functioning. Although prior research has primarily focused on disease-related risk factors, it is equally important to consider the potential influence of social-environmental factors, especially given the challenges associated with economic disadvantage that face many children with SCD. The goal of the present research is to examine the possible effects of social-environmental factors on cognitive function in this high-risk, yet understudied, population.

Sickle Cell Disease

Sickle cell disease (SCD) refers to a group of chronic genetic blood disorders that are among the most common inherited monogenic disorders in the world (Weatherall, Hofman, Rodgers, Ruffin & Hrynkow, 2005) and are characterized by recurrent pain crises, chronic anemia and other debilitating complications. SCD is caused by a genetic mutation resulting in the production of sickle hemoglobin (HbS), which causes red blood cells to become hard and abnormally shaped. There are several hemoglobinopathies in the SCD family with sickle cell anemia (HbSS) identified as the most common and the most severe. Other major types of sickle disease include hemoglobin SC disease (HbSC)

and hemoglobin S-beta thalassemia (Rees, Williams & Gladwin, 2010). SCD most commonly affects those of African descent, but cases have also been reported in those of Mediterranean, Indian and Arab descent (Driscoll, 2007).

In the United States, 44 states and the District of Columbia currently include hemoglobinopathy testing as part of newborn screening, which allows for early diagnosis before clinical manifestations. The first symptoms of SCD generally appear within the first year with disease presentation varying based on age. In early childhood, SCD patients are most likely to experience complications related to infection, spleen enlargement, and cerebrovascular damage. As patients enter adolescence and adulthood, they are more likely to suffer from retinopathy, leg ulcers, renal insufficiency, pulmonary hypertension, and other chronic organ damage. Some SCD complications, however, occur throughout the lifespan. The most common symptom of SCD is severe acute pain caused by the entrapment of sickled blood cells and the consequent interruption of blood flow. Considered the hallmark of SCD, vaso-occlusive pain crises are experienced by 70% of all patients and account for 30% of SCD-related hospital admissions. Acute chest syndrome (ACS) is another common complication of SCD and is caused by the obstruction of pulmonary vasculature. Symptoms of ACS include pain, fever, cough and hypoxia (Driscoll, 2007)

A recent report used United States census population data from each of the 50 states and the District of Columbia to estimate 89,079 people in the US living with an SCD disorder (Brousseau, Panepinto, Nimmer & Hoffmann, 2009). However, this number is likely an underestimation, as it includes the Black and Hispanic population but excludes White (including Mediterranean) and Asian (including Indian and Arab)

individuals. In the U.S., it is estimated that approximately one in less than 400 African-American newborns is affected with HbSS, HbSC or Hb S-beta thalassemia (Hassell, 2010). It is well established that individuals with SCD have a shortened life expectancy (e.g., Platt et al., 1994). However, due to improvements in screening and diagnostic procedures and advancements in treatment options, life expectancy has increased significantly over the last four decades. More specifically, life expectancy for individuals with sickle cell anemia (HbSS) has increased from approximately 14 years in 1973 to 42 years for males and 48 years for females in 1994 (Hamideh & Alvarez, 2013).

More recently, a study of 940 patients in the Dallas Newborn Cohort ranging in age from less than 1 month to 20 years, estimated the 18-year survival rate to be 93.9% for patients with more severe forms of the disease, such as HbSS, and 98.4% for patients with milder forms of SCD, such as HbSC (Quinn, Rogers, McCavit & Buchanan, 2010). This is an improvement from the estimated survival rates of the same cohort several years earlier (Quinn, Rogers & Buchanan, 2004). Hamideh and Alvarez (2013) observed a similar trend in SCD-related mortality. They found that, when compared to 1979-1998, SCD mortality during 1999-2009 significantly decreased by 61% for infants, 67% for young children and 22-35% for 5-19 year olds. Collectively, these studies show that, over the last several decades, survival has increased and mortality has decreased in children with SCD. It should be noted, however, that both studies show that these trends are not as encouraging for young adults who are actually at a greater risk for early SCD-related death than they were several years ago.

Hamideh and Alvarez (2013) suggest that certain barriers including limited access to providers, poor communication between providers, and insufficient insurance coverage

mark the transition period between pediatric and adult care. These findings demonstrate that more SCD patients are surviving through childhood while simultaneously struggling with the transfer of care between late adolescence and early adulthood. Consequently, there has been a push to redirect research efforts towards understanding if and how children with SCD are adapting to the psychosocial, psychological, and cognitive effects of living with the disease (Helps, Fuggle, Udwin & Dick, 2003).

Cognitive Function in Children with Sickle Cell Disease

Impaired cognitive function is one of the most significant negative developmental outcomes faced by individuals with SCD. Within the last three decades, there has been growing evidence that children with SCD experience cognitive deficits across several domains when compared to healthy peers and normative samples (e.g., Hijmans et al., 2011a; Schatz, 2004; Steen et al., 2005). In the most comprehensive meta-analysis to date, Schatz, Finke, Kellett and Kramer (2002) computed and compared the Cohen's *d* effect sizes for 14 previously published studies examining impairments in cognitive function in children with SCD. With regard to general intelligence, the authors found that the average IQ of children with SCD was 4.3 standard score points lower (d = -0.31) than that of healthy comparisons. The effect was notably larger for studies that also examined differences in specific cognitive areas. Seventy-one percent of the included studies found significant deficits in specific cognitive domains including attention, executive function, language and memory. No data were provided for the magnitude of the effects in these domains.

Since 2002, the body of research related to cognitive deficits in pediatric SCD patients has continued to grow with results generally replicating those found by Schatz et

al. (2002). Steen et al. (2005) found that pediatric SCD patients with normal magnetic resonance imaging (MRI) results (i.e., without any evidence of cerebrovascular damage) showed significant deficits in general intelligence when compared to healthy controls matched to patients by age, gender and race with a reported Cohen's *d* effect size of -.72. When all patients were considered, including those with MRI abnormalities, the effects were even greater with an overall Cohen's *d* effect size of -1.11. Additional analyses of patients with sickle cell anemia, the most severe form of SCD, showed that this group experienced the greatest impairment in tasks related to verbal intelligence. Hijmans et al. (2011a) found similar results, demonstrating that, on average, children with SCD obtained significantly lower IQ scores than controls matched by socioeconomic status (SES) with a mean full-scale IQ that was more than 1.5 standard deviations below population norms. More specifically, the authors reported that more than 1 in 3 children with SCD had an IQ lower than 75 standard points (the cut-off used for the identification of intellectual disability), compared to 1 in 10 children in the control group. They also found that children with SCD underperformed relative to controls in tasks related to both performance and verbal intelligence (Hijmans et al., 2011a). In a recent study of infants and toddlers living with SCD, patients scored, on average, a full standard deviation below population norms on a measure of cognitive development (Glass et al., 2013). These results suggest that functional deficits in cognition in children with SCD may begin at a very young age, placing patients at risk for early developmental delay.

In the years since the Schatz et al. (2002) meta-analysis, there has also been new evidence that children with SCD experience domain-specific cognitive impairment in areas such as memory, language, and executive function. For example, in an evaluation

of short-term memory, Schatz and Roberts (2005) found that children with SCD experienced significant difficulty in recalling auditory-verbal material when compared to demographically matched healthy controls. In a later study, Schatz and Roberts (2007) also found that toddlers and early preschoolers with SCD make more incorrect responses and perseverative errors on a delayed response working memory task. Additionally, there is evidence to suggest that children with SCD experience language-processing deficits that are not accounted for by tasks designed to measure verbal intelligence. For example, one study showed that children with the most severe cases of SCD significantly underperformed demographically matched healthy controls on semantic, syntactic and phonological tasks (Schatz, Puffer, Sanchez, Stancil & Roberts, 2009). Pediatric SCD patients also show subtle deficits in executive functions, including skills related to working memory, sustained attention, selective attention, and planning (Hijmans et al., 2011a). It has been proposed that the difficulties children with SCD experience with memory, language and executive function may be interrelated, specifically that memory and language impairments may be the result of executive dysfunction (Sanchez, Schatz & Roberts, 2010).

In addition to general intelligence and specific cognitive domains, researchers have also been interested in academic achievement and investigating the effect of these cognitive impairments on school performance. School-aged children with SCD tend to underperform relative to their peers on psychometric tests of academic achievement, which include tasks related to reading, writing and math (Schatz, 2002; 2004). More specifically, Schatz (2004) found medium effects on tests of reading decoding (r = -.31) and math calculations (r = -.37). While these findings are useful for detecting and

classifying functional impairments in students with SCD, a closer examination of non-psychometric outcome variables (i.e., measures of academic *attainment*) provides additional information. For example, a conservative estimate shows that more than 31% of students with SCD (44% when considering only participants who successfully enrolled in the study) received special services at school and/or had a reported history of grade retention. This estimate is compared to 14% of demographically matched comparison students recruited from the same community. Children with SCD were also more likely to repeat multiple grades with several participants repeating a grade past the third grade (Schatz, 2004). Furthermore, some evidence suggests that issues with academic achievement in children with SCD may begin at school entry. Steen et al. (2005) found that kindergarten students with SCD displayed deficits in certain kindergarten-readiness skills, which are generally required for future success in reading and math learning.

Another major finding from the last several decades of research into the cognitive development of children with SCD is that the magnitude of cognitive impairments appears to increase with age during childhood and adolescence. In the previously mentioned meta-analysis, Schatz et al. (2002) found that, after combining samples across the 14 included studies, the average IQ standard score decreased from 94.0 for 9-10 year olds to 85.6 for 10-11 year olds and again to 84.2 for 11-13 year olds. This pattern was not found among the comparison group, indicating that the difference in IQ between children with SCD and their healthy peers grows as the children age. However, given that the studies included in this meta-analysis utilized cross-sectional designs to determine age differences across different samples, the analysis is vulnerable to potential confounds. In a later single-study report of cognitive deficits in children with SCD, Steen

et al. (2005) found age was significantly negatively correlated with overall intelligence and explained approximately 11% of the variance in 1Q scores. The age-IQ correlation was also significant for verbal intelligence and approached significance for performance intelligence. More specifically, King et al. (2013) found that predicted full-scale intelligence declined by 0.96 points for every 1-year increase in age for pediatric SCD patients with a history of silent cerebral infarct. Age appears to play an important role in the cognitive development of toddlers as well, particularly for domain-specific abilities, including language and motor skills (Schatz & Roberts, 2007). While the effect of age on cognitive function in patients with SCD has been well studied throughout childhood, less is known about its effect during late adolescence and adulthood (Schatz et al., 2002).

Biomedical Predictors of Cognitive Impairment

Although it is well established that children with sickle cell disease are at risk for significant decrements in cognitive functioning, there is a limited understanding of the underlying causes. To date, most research has focused on the potential disease-related factors that appear to have a direct effect on cognition. One of the most highly studied among these factors is cerebral infarction, or stroke. Patients with SCD are at an increased risk of experiencing neurological damage, the most common and severe of which is the result of stroke. It is estimated that approximately 7% of children with sickle cell anemia will suffer from one or more overt cerebrovascular accidents before the age of 15 years, with incidence peaking between the ages of 2 and 5 years (Hogan, Pit-ten Cate, Vargha-Khadem, Prengler, & Kirkha, 2006; Schatz & Buzan, 2006). Pediatric SCD patients with a clinical history of overt stroke experience, on average, a 10-15 point

decline in IQ as well as difficulties with academic achievement and attainment (Schatz & McClellan, 2006).

It is important to note, however, that a significant percentage of children with SCD experience cerebral infarction without any overt symptoms, resulting in brain damage that is only detectable with MRI. Advancements in imaging technology have allowed for earlier and more accurate detection of these "silent" strokes, resulting in an estimated prevalence of 21.8% in children with SCD (Pegelow et al., 2002). While patients with a history of overt stroke are typically at the greatest risk for cognitive impairment, there is evidence that children with MRI-detected silent strokes are also vulnerable to mild deficits in cognitive function in comparison to both SCD patients with no MRI abnormalities and healthy controls (e.g., Brown et al., 2000; King et al., 2014; Hogan et al., 2006).

Given that pediatric SCD patients without a history of cerebral infarction, either overt or silent, also experience notable cognitive impairment (e.g., Brown et al., 2000; Hogan et al., 2006), it is important to consider the impact of other biomedical factors. One such factor is peak cerebral blood flow (CBF) velocity. Children with SCD with normal MRI results but *abnormal* CBF perform poorly on measures of language functioning, general intelligence and attention (Sanchez, Schatz & Roberts, 2010; Strouse et al., 2006). This is the result of an inverse relationship, such that increased CBF velocity is associated with decrements in cognitive function. As might be expected, CBF velocity is closely tied to occurrence of stroke in SCD patients and has been utilized to identify those with the highest risk.

CBF is also related to sleep-disordered breathing, another important disease-related predictor of cognitive function in this population (Hill et al., 2006). One estimate suggests that as many as 40% of children with SCD are affected by sleep-disordered breathing, which results in frequent sleep disruption and nocturnal oxygen desaturation (Needleman et al., 1999). Research with non-SCD patients has shown that children with obstructed breathing during sleep experience subtle but significant impairments in processing speed, attention, and executive function (e.g., Beebe et al., 2004; Hill et al., 2006). In a recent study with children with SCD, Hollocks et al. (2012) found that sleep-disordered breathing, which is associated with low hemoglobin oxygen saturation, may negatively impact general intelligence and specific executive domains.

Another reported biomedical predictor of cognitive function in young SCD patients is anemia severity. Anemia, or a decrease in the number of red blood cells, is one of the hallmark conditions associated with sickle cell disease. Evidence suggests that anemia severity, which is determined by hemoglobin level, is inversely correlated with performance on certain domains of cognitive function, including short-term and working memory, verbal comprehension, and overall intelligence (Hijmans et al., 2011b; Steen et al., 2003). In one case, Steen and colleagues (2003) found that anemia explained 23% of the variance in overall IQ in pediatric SCD patients without a history of stroke. As with sleep-disordered breathing, these effects are likely due to insufficient cerebral oxygenation.

Collectively, these findings demonstrate the major impact that disease-related factors have on the cognitive development of children with SCD. Nevertheless, biomedical characteristics of the disease only explain a portion of the variance in

children's cognitive function. This suggests that there may be other important, but not yet explored factors contributing to the observed effect.

Social-environmental Predictors of Cognitive Impairment

To date, research on cognitive impairment in children with SCD has primarily focused on the disease-related risk factors discussed above. Although there is evidence to suggest that social-environmental factors such as income and home environment may also be implicated in children's cognitive development, these issues have received little attention in SCD research in comparison. In a recent study, King et al. (2013) found that while biologic factors such as cerebral infarction and hemoglobin oxygen saturation played a significant role in the cognitive function of children with SCD, a considerable amount of the additional variance was due to social-environmental factors such as parental education and family income. This suggests that the underlying causes of cognitive impairment in children with SCD may be complex and multidimensional in nature.

For 2012, the United States Census Bureau reported a poverty threshold of $23,283 for households with two adults and two children. While the national poverty rate was 15%, the African American population was disproportionately represented with more than one fourth (27.2%) of all Black individuals and families living in poverty. In the same year, 41.2% of all families headed by a single, Black female lived in poverty (DeNavas-Walt, Proctor & Smith, 2013). These statistics have troubling implications for the predominantly Black population of SCD patients and their families. Indeed, many individuals with SCD experience poverty and chronic financial hardship (Barbarin, Whitten, Bond & Conner-Warren, 1999a). Interestingly, there is evidence to suggest that

patients and families with SCD may be more socioeconomically disadvantaged when compared to the larger U.S. Black population (USBP). Specifically, Farber, Koshy and Kinney (1985) found that the median family income for patients with SCD was significantly less than that of the USBP. The authors also showed that 40% of SCD patients came from two-parent households and 53% came from households headed by a single female compared to 54% and 42%, respectively, for all African Americans. Additionally, children with SCD are more likely to come from high-stress, chaotic homes characterized by disorganization and family conflict (Burlew, Evans & Oler, 1989).

There is an extensive body of research demonstrating the damaging effects of chronic poverty on neurodevelopment and cognitive development. In their review of the relationship between socioeconomic status and brain development, Hackman and Farah (2009) described pronounced economic disparities in several areas of cognitive ability, including language ability, executive function and memory which are associated with the left perislvian, prefrontal, and medial temporal brain regions, respectively. Findings on the effect of economic deprivation on other domains, including visual/spatial cognition are inconclusive, suggesting that financial hardship affects the various neurocognitive systems differently (Farah et al., 2006; Hackman & Farah, 2009).

The impact of growing up in persistent poverty is also apparent through more global measures of cognitive ability, such as IQ. One report showed that low-income children as young as 5 years old were already underperforming compared with their more affluent peers on tasks related to verbal intelligence, performance intelligence, and overall intelligence (Duncan, Brooks-Gunn & Klebanov, 1994). On average, children raised in poverty obtain IQ scores 5-10 points lower than those of children raised in

middle class families (Kaiser & Delaney, 1996). The growing literature on the relationship between economic status and academic achievement has produced similar results. In a meta-analytic review of articles published between 1990 and 2000, Sirin (2005) calculated medium to strong effects, with children raised in poorer families or attending disadvantaged schools experiencing greater academic difficulty. It is important to acknowledge that exposure to persistent poverty during childhood has lasting effects, predicting cognitive impairment not only in the present, but also well into adulthood (Kaplan et al., 2001). Collectively, this evidence suggests that children with SCD, who are already experiencing disease-related effects on cognitive ability, may be facing a double hit due to the disadvantaged conditions in which they grow up.

In an effort to better comprehend the mechanism through which poverty and home environment impact cognitive development in children, the field has turned its attention to parenting as a possible mediator. Kaiser and Delaney (1996) refer to the parent-child relationship as "the primary developmental context in which early cognitive, social, and behavioral development will occur." Indeed, there is evidence to suggest that parenting styles and behaviors are implicated in cognitive development of offspring (e.g., Lugo-Gil & Tamis-LeMonda, 2008; Tamis-LeMonda, Shannon, Cabrera, & Lamb, 2004).

However, before one can comprehend how economic disadvantage affects the parent-child relationship, it is crucial to understand how poverty directly affects parents as individuals. Parents raising families in impoverished conditions are often faced with the challenges of unemployment, racial discrimination, health issues, and a lack of vital resources including food, water and heat (Guo & Harris, 2000). Additionally, low-income

parents more frequently report low levels of familial and community support (Middlemiss, 2003). In a comprehensive review of the literature, Kaiser and Delaney (1996) state that persistent exposure to financial hardship and limited social support is associated with chronic psychological distress in parents, including elevated rates of depression, maladjustment and overall behavioral instability. Others refer to the prolonged stress of economic disadvantage as a source of allostatic load, which, over time, wears on parents, resulting in the expression of negative emotional states (Bradley & Corwyn, 2002). In either case, this adverse psychological context harbors secondary affects of poverty on the parent, including increased expression of frustration, aggression, withdrawal and, in general, weakened interpersonal relationships.

More specifically, this prevailing context of negative emotionality is likely to compromise a parent's ability to engage in healthy relationships with their children. Indeed, research has shown that socioeconomically disadvantaged adults engage in parenting behaviors that are harsh and coercive and lacking in consistency, support, and sensitivity to children's needs (e.g., Hackman, Farah & Meaney, 2010; Kaiser & Delaney, 1996, Luby et al., 2013). From a broader perspective, these parents tend to value punitive parenting styles that emphasize obedience and conformity, while more affluent parents are likely to emphasize self-confidence and self-direction (Kaiser & Delaney, 1996; Leyendecker, Harwood, Comparini & Yalcinkaya, 2005).

These patterns of parenting styles and values often manifest themselves indirectly via impaired parent-child interactions. For example, Hart and Risley (1995) found that parents with lower incomes use less complex and diverse language when interacting with their children. Such communication styles are typically associated with parenting

behaviors that are less nurturing and less responsive (Hart & Risley, 1995). This is consistent with findings from Guo and Harris (2000) who showed that exposure to poverty exerted a strong negative effect on parent-child interactions, such that disadvantaged mothers were less likely to engage in recurrent conversation with their child and were less likely to answer their child's questions with verbal responses.

Evans and colleagues have studied the concept of parental responsiveness extensively, demonstrating that psychological stress, limited social support and chaotic home environments mediate the relationship between poverty and responsiveness (Doan & Evans, 2011; Evans, Boxhill & Pinkava, 2008; Evans et al., 2010). Conversely, the resilience displayed by certain children raised in chronic high-stress environments may be attributed to parenting that is responsive and attuned to the child's needs. More specifically, Doan and Evans (2011) suggest that mothers who are highly responsive are more likely to exhibit child-centered teaching skills and create a more enriching environment. In addition to stimulating cognitive development, these types of parenting behaviors may also indirectly compensate for the direct effects of long-standing poverty and stress on children's functioning (Doan & Evans, 2011). Additionally, the work produced by Evans and colleagues has emphasized the relationship between duration of poverty and cumulative risk exposure. In other words, the longer children are exposed to poverty, the greater their accumulation of adverse physical (e.g., crowding, noise, substandard housing) and psychosocial (e.g., family discord, violence) risk factors. Over time, this is related to greater distress and more impaired functioning for both children and parents (Evans, 2003; Evans & Kim, 2007). This temporal affect suggests that

children with sickle cell disease, who are already susceptible to a decline in cognitive function with age, may be facing a double hit over time.

Importantly, when considering the impact of poverty and parenting on cognitive development in children with sickle cell disease, one must also consider the additional stress exerted on parents when raising a child with a life-threatening, chronic illness. For example, Brown et al. (2008) posit that parents of chronically ill children are exposed to a number of different stressors including financial strain, disruptions to daily routine and an increase and shift in caretaking responsibilities. In the context of SCD, research has shown that there is a significant inverse relationship between disease-related parenting stress and family functioning among families with children with SCD, particularly in the area of communication (Barakat, Patterson, Tarazi & Ely, 2007). Consistent with the findings reported above, family income was also a significant predictor of disease-related parenting stress. These results suggest that parents of children with sickle cell disease, many of whom are also socioeconomically disadvantaged, may be facing a double hit to their capacity to be warm, supportive, and responsive parents.

Present Research and Hypotheses

The current literature has firmly established that children with sickle cell disease are at risk for considerable cognitive impairment across several domains. Given that the life expectancy for SCD patients is on the rise and that more pediatric patients are surviving into adulthood, there is a push in research to identify the underlying mechanisms responsible for these decrements in cognitive function. Prior research has focused on potential disease-related risk factors (e.g., cerebral infarction, cerebral blood flow velocity, sleep-disordered breathing, anemia severity) and their effect on cognition.

A separate, but related, body of research provides evidence to suggest that social-environmental factors such as income and home environment may also be implicated in the cognitive development of children with SCD. However, few studies have specifically examined these potential effects within this high-risk population.

Past research with non-SCD patients and families has provided a sufficient backdrop upon which we may begin to form hypotheses about how social-environmental factors might affect children with SCD. As highlighted above, chronic exposure to financial hardship is associated with poorer cognitive function in children, a relationship that appears to be mediated by parenting behaviors. Given the particular demographic characteristics of children with SCD and their families (i.e., largely African American, low-income), it is important to understand the relationship between social-environmental stress, parenting and child cognitive function in this complex, underrepresented population. By identifying those parenting behaviors that may be adverse and those that may be protective, this research may help inform future interventions aimed at improving parent-child interactions and cognitive function in children with SCD.

The purpose of the present research is to extend the existing literature on social-environmental stress, parenting and cognitive function and to unite these concepts in the context of pediatric sickle cell disease. I will examine how certain sociodemographic factors are related to parenting and if they serve as unique predictors of cognitive function in children with SCD. I will do so by exploring the following questions and hypotheses:

1. How do children with sickle cell disease compare to their same-age peers on measures of cognitive function?

    a. Hypothesis: Children with SCD will underperform the normative sample on measures of cognitive function, including those in the domains of intelligence, academic achievement, and executive functioning.

2. Is the cognitive functioning of children with SCD stable over a period of 12-24 months?
    a. Hypothesis: Over time, children with SCD will show a decline in performance on measures of cognitive function, including those in the domains of intelligence, academic achievement, and executive functioning.
3. Are social-environmental stressors related to maternal psychological distress and parenting behaviors?
    a. Hypothesis: Higher levels of social-environmental stress will be associated with higher levels of maternal distress and lower levels of positive parenting behaviors.
    b. Exploratory analyses will determine how various social-environmental stressors (including household constellation, financial stress, racial discrimination stress, home routine and home chaos) are related.
4. Are maternal social-environmental stress, psychological distress and parenting related to cognitive functioning in children with SCD?
    a. Hypothesis: Higher levels of maternal stress and distress and lower levels of positive parenting will be associated with lower levels of cognitive functioning in children with SCD.

b. Exploratory analyses will determine if stress, distress and parenting serve as unique predictors of children's performance on measures of cognitive function.

CHAPTER II

METHOD

The present study was conducted as a part of a larger, prospective cohort study, Cognition in Children with Sickle Cell Anemia (COCCA), with the aim of determining if cognitive function and school outcomes of children with sickle cell disease change over time (King, 2006). The COCCA study protocol was approved by the Institutional Review Board at the Washington University School of Medicine. Informed consent or assent was obtained from each participant prior to study entry and participation.

Participants

Participants were 65 children and their mothers. All eligible participants were presently receiving treatment at the Sickle Cell Clinic at St. Louis Children's Hospital. This specialty clinic is part of the Pediatric Division of Hematology at Washington University School of Medicine, which follows approximately 350 children with sickle cell disease, of which roughly 200 are school-aged. Inclusion criteria for participants in the present study included (a) a diagnosis of SCD confirmed by hemoglobin analysis; (b) current enrollment in school; (c) documented brain magnetic resonance imaging (MRI) at 5 years of age or older; and (d) completion of the neuropsychological battery at Time 1 (T1) as part of their participation in the study.

Demographic characteristics of the pediatric SCD patients in the sample at time of enrollment are shown in Table 1. Children ranged from ages 6 to 16 years old (M = 11.23; SD = 3.21). Participants represented a variety of sickle cell disease subtypes: more than half of the sample (54%) was diagnosed with HbSS, which is typically the most severe type. Another 25.4% and 20.7% were diagnosed with HbSC and variations of

hemoglobin S-beta thalassemia, respectively. Evaluation of patient MRI studies by a trained neuroradiologist revealed that the majority of children (95.2%) displayed no evidence of a cerebral infarct. The remaining 4.8% displayed evidence of silent infraction. With regard to school, children missed an average of 24.37 days (*SD* = 22.07) in the last year. Examination of participants' school records showed that 25.9% of the sample had repeated a grade, 26.3% had an Individualized Education Program in place, and 14% had an established 504 plan.

Demographic characteristics of the mothers in the sample at time of enrollment are shown in Table 2. This information was self-reported on a brief, supplemental questionnaire. Mothers ranged in age from 27 to 59 years old (*M* = 37.71; *SD* = 6.46). Approximately half of the sample (56%) attended some college or trade school. The majority of participants (82.4%) were employed outside of the home and earned an average monthly income of $2,051. 11.5% of participants were not employed. On average, participants had 2 biological children (*M* = 2.3; *SD* = 0.9) and reported living in households of approximately 4 people (*SD* = 1.41).

Measures

Intelligence. Children with SCD completed the Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler, 1999). The WASI is widely used to assess intelligence in children and adults. The measure consists of four subtests: Block Design, Vocabulary, Matrix Reasoning and Similarities. The total combined performance on these subtests is used to generate the Full-Scale Intelligence Quotient (FSIQ), a broad estimate of general intellectual ability. It is also possible to interpret subtest scores based on specific components of intelligence including performance intelligence and verbal intelligence.

The Verbal Intelligence Quotient (VIQ) is comprised of the Vocabulary and Similarities subtests and is designed to measure verbal comprehension. The Performance Intelligence Quotient (PIQ), comprised of the Block Design and Matrix Reasoning subtests, is intended to assess non-verbal intellectual abilities, specifically perceptual organization of visual stimuli.

Academic achievement. Children with SCD also completed several tests from the Woodcock-Johnson-III Tests of Achievement (WJ-III; Mather & Woodcock, 2001). The WJ-III is a system of 22 tests designed to measure a variety of academic skills in reading, mathematics, writing and oral language in school-aged children. The COCCA neuropsychological battery included five such tests from the WJ-III: Math Fluency, Reading Fluency, Letter-Word Identification, Calculations and Spelling. Reading Fluency and Letter-Word Identification are designed to assess a variety of reading skills including decoding, speed and semantic processing. The Math Fluency and Calculations tests are an assessment of number facility, automaticity, and overall achievement in mathematics. Finally, performance in Spelling demonstrates achievement in basic writing skills.

Executive function. Children also completed several tests from the Delis-Kaplan Executive Function System (D-KEFS; Delis, Kaplan & Kramer, 2001). The D-KEFS consists of 9 tests designed to measure verbal and spatial (non-verbal) components of executive function in children and adults. The present study's neuropsychological battery included the Trail Making, Verbal Fluency, Color-Word Interference and Sorting tests from the D-KEFS. Collectively, these tests assess a variety of executive function domains such as flexibility, sequencing, shifting, and inhibition.

Additionally, mothers of children with SCD completed the Behavior Rating Inventory of Executive Function (BRIEF; Gioia, 2000). The BRIEF is a paper questionnaire administered to caregivers to assess a variety of executive function behaviors. For each of the 86 items, mothers indicated whether that behavior was never, sometimes, or often a problem for their child within the last month. The scored questionnaire generates two validity scales and eight clinical scales including Inhibit, Shift, Emotional Control, Initiate, Working Memory, Plan/Organize, Organization of Materials and Monitor. When interpreted together, these eight scales form the Global Executive Composite (GEC), an overall index of executive function.

Maternal social-environmental stress. Mothers of children with SCD reported on the frequency and/or magnitude of several potentially stressful social-environmental factors. Responses were solicited by a trained research assistant as an orally presented parent interview with computer-assisted personal interviewing. Several domains of social-environmental stressors were assessed:

(1) *Financial stress.* The strain associated with income and mothers' ability to provide essential resources for their families was measured as a composite of reported monthly income and scales derived from a measure created by Murry et al. (2008). Participants were asked a series of questions regarding their present financial situation to determine ability to make ends meet (e.g., how much difficulty have you had paying your bills during the past 12 months) as well as the extent of any unmet material need (e.g., we have enough money to afford the kind of food we need; we have enough money to afford the kind of medical care we need).

(2) *Racial discrimination stress.* Mothers of children with SCD also completed 9 items derived from the revised version of the Schedule of Racist Events (SRE; Landrine & Klonoff, 1996). The SRE was designed for use with adults, but has been successfully revised for use with youths and adolescents (Brody et al., 2006). These items determine the frequency with which participants encounter a number of racially biased situations (e.g., how often have you been treated rudely or disrespectfully because of your race). For each item, participants were asked to report if the situation never happened, happened sometimes, or happened a lot.

(3) *Household constellation.* Participants were asked to report the number of biological children currently living in the home. This information was used as a proxy to determine the size and general arrangement of the household.

(4) *Home routine & chaos.* The interview also included a series of items related to home routine and home chaos based on a home environment scale (Evans et al., 2005). This instrument is designed to measure the degree of planning (e.g., we have an evening bed time routine with [child]) and order (e.g, there is very little commotion in our home, we can talk to each other without being interrupted) present in the participant's household.

Maternal psychological distress. Within the parent interview, mothers completed the Center for Epidemiologic Studies Depression Scale (CES-D; Radloff, 1977). The CES-D is a 20-item self-report measure designed to assess depressive symptoms in adults. For each item, participants report how often they have experienced a number of emotions and behaviors over the last week on a scale ranging from 0 (rarely or none of the time) to 3 (most or almost all of the time). The CES-D covers a range of depressive

symptoms, including sadness, hopelessness, loneliness, altered appetite, abnormal sleep, etc.

Maternal positive parenting. Positive parenting behaviors were assessed as part of the previously mentioned parent interview based on questions constructed by Brody et al. (2001). Mothers were asked to use a 4-point scale to indicate how often they engaged in two specific components of positive parenting: consistent discipline and child monitoring. Consistent discipline refers to the mother's ability to maintain and adhere to previously established rules regarding the child's behavior (e.g., how often do you discipline [child] for something at one time, and then at other times, not discipline him/her for the same thing). Child monitoring refers to the mother's knowledge regarding events and activities in the child's daily life (e.g., how often do you know when [child] does something really well at school or someplace else away from home). Mothers reported the general frequency of these behaviors on a scale ranging from 1 (never) to 5 (always). Responses were scored and aggregated to create a combined index of positive parenting.

Procedure

Mothers of eligible children with SCD were identified and approached in the outpatient Sickle Cell Clinic at St. Louis Children's Hospital by a trained member of the research team. After introducing the study, a staff member contacted interested mothers to schedule the first evaluation (Time 1, T1). During the T1 evaluation, mothers and children provided informed consent and assent, respectively. Next, children completed the neuropsychological testing battery while mothers completed the BRIEF and the additional questionnaires included in the parent interview. T1 evaluations typically lasted

3-4 hours. As compensation for their involvement in the study, participants received gift cards to local retail stores. Mothers were contacted at a later date to schedule the second evaluation (Time 2; T2), which occurred, on average, 12-24 months after T1.

Statistical Analyses

Means and standard deviations of the WASI, WJ-III, D-KEFS and BRIEF were calculated. Additionally, one-sample *t*-tests were used to compare pediatric SCD patients' performance on these measures to that of the normative sample. Pearson correlations were calculated to determine associations between measures of children's cognitive function, maternal social-environmental stressors, maternal psychological distress, and positive parenting. The impact of maternal social-environmental stress, distress and positive parenting on children's cognitive function was evaluated using linear multiple regression analyses. Finally, paired sample *t*-tests were used to compare T1 and T2 cognitive function to identify significant changes in performance over time.

CHAPTER III

RESULTS

Preliminary Analyses

Data Reduction. In order to reduce the number of analyses conducted, variables that were measuring similar constructs and were sufficiently intercorrelated were combined to create composite variables. Comparisons of the Letter-Word Identification, Reading Fluency, Calculations, Math Fluency and Spelling tests of the WJ III are shown in Table 4. All tests were significantly correlated ($p < .001$). Therefore, children's scores on these tests were averaged to create a composite academic achievement variable. Comparisons of variables related to home environment are presented in Table 5. Number of children in the home, number of biological children and number of people in the home as reported by mothers were all significantly correlated ($p < .001$). However, supplementary correlational analyses revealed that the number of children in the home and the number of people in the home were not significantly associated with other outcome variables. Thus, number of biological children was selected as a proxy to represent household constellation in the subsequent analyses. The home routine and home chaos variables, which were not significantly correlated with other home environment variables, were examined independently in the analyses. Table 6 shows the correlations of variables related to maternal economic status. Monthly income, ability to make ends meet and extent of unmet material need were significantly correlated ($p < .001$). Thus, mothers' scores on these variables were averaged to create a composite financial stress variable.

Descriptive Analyses. Children with sickle cell disease were compared to the normative sample of same-age peers on the cognitive function measures. The results, presented in Table 3, indicate that children with SCD significantly underperformed the normative sample on a variety of domains related to intelligence, achievement, and executive functioning. Pediatric SCD patients scored significantly lower on all indices of the WASI, which included verbal intelligence, t (58) = -2.47, p = .02, performance intelligence, t (58) = -4.98, p < .001, and full-scale IQ, t (58) = -4.01, p < .001. Children with SCD also scored significantly below average on the Letter-Word Identification, t (57) = -1.98, p = .05, Reading Fluency, t (52) = -5.74, p < .001, Calculations, t (55) = -2.91, p = .01, and Math Fluency, t (53) = -7.53, p < .001, tests of the WJ-III. There was no significant difference on the Spelling test of the WJ-III.

The results were mixed for both mother-reported and observed measures of executive function. On the BRIEF, mothers reported that their children with SCD experienced significantly more problems with initiating tasks, t (58) = 3.25, p = .002, planning and organizing, t (59) = 3.99, p < .001, and working memory, t (58) = 5.32, p < .001. These elevated scale scores were also reflected in the above average Metacognition Index, t (58) = 4.07, p < .001, and Global Executive Composite, t (58) = 2.85, p = .006, scores. On the D-KEFS, pediatric SCD patients scored significantly lower than the normative sample on some conditions of the Trails task, including Visual Scanning, t (37) = -2.74, p = .009, and Number/Letter Switching, t (37) = -3.93, p = < .001, as well as the Color/Word Interference task, including Inhibition, t (37) = -2.83, p = .008, and Inhibition Switching, t (37) = -3.65, p = .001. There were no significant differences

between children with SCD and the normative sample on any conditions of the Verbal Fluency or Card Sorts tasks.

Correlational Analyses: Social-Environmental Stress, Psychological Distress, Parenting and Cognitive Function

Correlations among the measures of child cognitive function, maternal social-environmental stress, maternal psychological distress and positive parenting are presented in Table 7. As expected, all three indices of the WASI were significantly positively correlated. Additionally, Achievement was significantly positively correlated with VIQ (r = .73, p < .001), PIQ (r = .60, p < .001) and FSIQ (r = .75, p < .001). Executive function was negatively associated with academic achievement (r = -.31, p = .02), such that lower WJ-III scores are related to greater executive function impairments as measured by the BRIEF. The relationship between executive function and FSIQ approached statistical significance (r = -.19, p = .14). However, executive function was not significantly related to either VIQ or PIQ.

Exploratory correlational analyses determined that measures of social-environmental stress were largely uncorrelated, with the exception of financial stress, which was significantly positively associated with household constellation (r = .30, p = .03). Maternal psychological distress, as measured by depressive symptoms on the CES-D, was significantly positively correlated with both financial stress (r = .68, p < .001) and racial discrimination stress (r = .38, p = .007). Positive parenting shared a significant positive relationship with home routine (r = .36, p = .01), such that more positive parenting is associated with more routine and structure in the home environment. Positive parenting was also negatively correlated with financial stress (r = -.32, p = .03), but was

not significantly related to household constellation, home chaos, or racial discrimination stress.

Results of the correlational analyses between child cognitive function and maternal stress and distress were mixed. More specifically, maternal financial stress was significantly negatively correlated with children's VIQ (r = -.35, p = .01), FSIQ (r = -.29, p = .04), and achievement scores (r = -.36, p = .01). Financial stress also shared a significant positive relationship with executive function (r = .34, p = .02). There was no significant association between maternal financial stress and children's PIQ scores. Home routine was significantly negatively associated with executive function (r = -.28, p = .05), such that more routine and structure in the home environment was related to fewer executive function problems in children as measured by the BRIEF. Household constellation, home chaos and racial discrimination stress were not significantly related to intelligence, achievement or executive function in children with SCD. It should be noted, however, that the negative relationship between maternal racial discrimination stress and child academic achievement approached significance (r = -.22, p = .13). Maternal depression was significantly positively correlated with executive function problems (r = .56, p < .001) and negatively correlated with academic achievement (r = -.28, p = .05). While maternal depression was not associated with PIQ or FSIQ, the correlation with VIQ trended towards significance (r = -.24, p = .10).

Finally, Table 7 also indicates that positive parenting is significantly negatively correlated with children's impairments in executive functioning (r = -.54, p < .001). Positive parenting was not significantly related to intelligence or academic achievement in children with SCD.

Linear Regression Analyses

A series of linear multiple regression analyses were conducted to further explore how maternal social-environmental stress, psychological distress and positive parenting might account for variability in cognitive functioning in children with sickle cell disease. In each regression analysis, financial stress, household constellation, and racial discrimination stress were entered in Step 1, Step 2 and Step 3, respectively. This was followed by maternal depression, which was entered in Step 4 and positive parenting entered in Step 5. FSIQ was entered as a dependent variable in the first regression. The results, which are presented in Table 8, show that financial stress approached significance in Step 1 (β = -.26, p = .10) and Step 2 (β = -.29, p = .10) and reached significance as a predictor of FSIQ in Step 3 (β = -.30, p = .05). Financial stress no longer remained significant in Step 4 or Step 5 of the model. No other variables accounted for FSIQ in this model.

To better understand the potential differences between performance and verbal intelligence, PIQ and VIQ were entered as dependent variables in the following analyses. In the model predicting PIQ scores (see Table 9), none of the entered variables significantly accounted for differences in children's performance intelligence. However, in the model predicting VIQ scores (see Table 10), financial stress was a significant predictor in Step 1 (β = -.32, p = .03), as well as Step 2 (β = -.34, p = .02) and Step 3 (β = -.34, p = .03). Financial stress approached significance in Step 4 (β = -.30, p = .13) and no longer remained significant in Step 5 of the model. No other variables accounted for VIQ in this model.

A similar trend occurred in the regression model predicting academic achievement. The results, which are presented in Table 11, show that financial stress was a significant predictor in Step 1 (β = -.34, p = .02), as well as in Step 2 (β = -.35, p = .02) and Step 3 (β = -.31, p = .04). Financial stress approached significance in Step 4 (β = -.29, p = .13) and no longer remained significant in Step 5 of the model. No other variables accounted for academic achievement in this model.

Executive function was entered as a dependent variable in the final regression (see Table 12). As with the previous analyses, financial stress was a significant predictor in Step 1 (β = .38, p = .007), and again in Step 2 (β = .40, p = .006) and Step 3 (β = .40, p = .007). Financial stress no longer remained significant in Step 4, whereas maternal depression proved to be a significant predictor (β = .65, p = .001). In Step 5, positive parenting partially accounted for executive function (β = -.29, p = .04), while maternal depression also remained significant (β = .46, p = .02). Household constellation and racial discrimination stress did not account for children's executive function during any step in this model.

Changes in Cognitive Function at Follow-Up

A series of paired sample *t*-tests were conducted to examine the stability/change of cognitive function in children with sickle cell disease between their first neuropsychological assessment and a follow-up assessment 12-24 months later. The results are presented in Table 13. Scores on the Letter-Word Identification and Spelling tests of the WJ-III declined an average of 3.19 points, t (36) = 3.16, p = .003, and 2.92 points, t (36) = 3.54, p = .001, respectively, at follow-up. The mean decline of 2.39 points on the Calculations test approached significance, t (35) = 1.70, p = .10. The differences in

scores at T1 and T2 were not significant for the Reading Fluency and Math Fluency tests of the WJ-III.

On the BRIEF (mother reports of problems in executive function), children with SCD had significantly fewer problems in the Emotional Control, t (37) = 2.02, p = .05, and Initiate, t (38) = 2.77, p = .009, domains. Children's decline in problems in the Monitor domain approached significance, t (38) = 1.84, p = .07. This multi-domain change in executive function corresponded to significantly fewer problems on the Metacognition Index, t (37) = 2.05, p = .05, and a trend towards significance on the Behavioral Regulation Index, t (37) = 1.75, p = .09.

Results for the observed measure of executive function were mixed. On average, children with SCD scored 8.35 points lower on the Visual Scanning condition of the Trails test at T2 than at T1, t (19) = 2.44, p = .02. Scores also declined on the Inhibition condition of the Color/Word Interference test by a mean of 3.43 points, t (20) = 1.86, p = .08, which trended towards significance. However, children demonstrated improved performance on the Switching Accuracy condition of the Verbal Fluency test, t (20) = -1.62, p = .12, and Motor Speed condition of the Trails test, t (20) = -1.89, p = .07, which approached significance. Scores on the other conditions of the D-KEFS tests remained relatively stable between assessments.

Finally, scores on the VIQ, PIQ and FSIQ indices also remained relatively stable when re-assessed at follow-up (i.e., there were no significant differences in scores on these measures at T1 and T2).

CHAPTER IV

DISCUSSION

The purpose of the present study was to build upon and extend the findings from the current body of research on social-environmental stress, parenting and cognitive function within the scope of pediatric sickle cell disease. It has been well established that children with SCD are at risk for significant impairments in intelligence, executive function, academic achievement, and other domains of cognitive function (e.g., Schatz et al., 2002). Simultaneously, a separate body of research with non-SCD populations has shown that social environmental factors such as income and home environment are related to cognitive development in children, a relationship that appears to be mediated by parenting behaviors. This is a particularly salient concern for children with SCD and their families given their distinct demographic characteristics (i.e., largely African American, low income). Thus, I aimed to assess if and how certain social-environmental factors are related to parenting and if these factors serve as predictors of various domains of cognitive function in children with sickle cell disease. I was also interested in examining how these children compare to their typically developing peers in terms of cognitive function and if their performance on cognitive function measures remains stable over time. These findings may help guide the development of interventions to help improve cognitive function in children with SCD by encouraging greater use of positive parenting behaviors.

In the current sample, children with sickle cell disease significantly underperformed relative to the normative data on same-age peers on measures assessing intelligence, achievement and executive function. On a widely used measure of overall

intelligence, children scored significantly lower than national norms on all indices, including verbal intelligence and global intelligence. On the performance intelligence scale, children with SCD obtained a mean score nearly 10 standard score points below average, reflecting an effect size of approximately two-thirds of a standard deviation. This is consistent with previous findings demonstrating significant impairment in pediatric SCD patients across all indices of intelligence (e.g., Hijmans et al., 2011a). It is worth noting that while some studies show children with SCD experience greater impairment on tasks related to performance intelligence (as was the case in the present study), others show that the greatest impairment occurs on tasks related to verbal ability. In future research, it will be important to determine if these variations are due to group differences (e.g., age, disease severity) and if greater impairment in a certain domain is related to poorer outcomes in this population.

Children's mean scores on several tests of academic achievement were also considerably lower than the normative sample means, including tests of Letter-Word Identification, Reading Fluency, Calculations and Math Fluency. This is consistent with and extends previously reported findings that pediatric SCD patients significantly underperform healthy students on tests of reading decoding and math calculations (Schatz, 2004). Collectively, these results suggest that school performance is a specific domain of functioning implicated in the broader cognitive impairment experienced by many children with sickle cell disease.

Executive function is another domain that appears to be affected by wide-reaching cognitive impairment in children with sickle cell disease. Problems with higher-order cognitive processes were observed across two different methodologies. Mothers reported

that their children with SCD experienced greater difficulty with starting tasks and generating behaviors (Initiate), holding and manipulating information in mind (Working Memory), and setting goals and ordering information (Plan/Organize). Importantly, while the mean scores for this sample on these BRIEF scales were not within the clinical range (*T* score at or above 65) and were not elevated to the point of immediate clinical concern, it is still worthwhile to note that children with SCD may be facing executive dysfunction when compared to their typically developing peers. Deficits were also observed on a performance-based measure of executive function. In particular, children with SCD demonstrated significant impairment on D-KEFS tasks related to sequencing and shifting (Trail Making) and inhibition (Color-Word Interference). Collectively, these results provide evidence for observed and reported deficits across many, but not all, domains of executive functioning.

In addition to completing the baseline assessment described above, participants returned for a follow-up neuropsychological assessment, which occurred, on average, 12-24 months later. Partial support was found for the second hypothesis, with children with SCD showing marked decline on certain measures of cognitive function while showing stability, or even improvement, on others. Mean performance on all three indices of general intelligence remained relatively stable over time. However, there was greater variation in change among tests of academic achievement. More specifically, children with SCD experienced significant declines over time on the Letter-Word Identification and Spelling tests of the WJ-III, while scores on the Reading Fluency, Math Fluency and Calculations tests did not differ considerably between assessments. These results are inconsistent with past findings demonstrating that cognitive impairment, particularly in

the domain of general intelligence, worsens with age in this population (e.g., Schatz et al., 2002; Steen et al., 2005). It is possible that the timeframe chosen for the follow-up assessment in the present study was not sufficiently sensitive in detecting potential declines in participants' intelligence. In a recent study, King et al. (2013) found a mean decline of 0.96 standard score points in IQ for every year a child with SCD ages. This suggests that the mean time between baseline and follow-up assessment in the present study might not have been large enough to capture statistically significant changes in performance.

Notably, several domains of observed and mother-reported executive functioning improved or remained relatively stable at the follow-up assessment, with the exception of the Visual Scanning condition of the D-KEFS Trail Making test, on which children with SCD experienced a significant decline in performance. Given that the majority of research on the longitudinal trajectory of cognitive function in pediatric SCD patients has focused on measures of general intelligence, less is known about the expected development of executive skills in this population. Additionally, scores derived from the D-KEFS, an observed measure of executive function, are based solely on participant performance and research has observed significant practice effects across most subtests of the D-KEFS (Homack, Lee & Riccio, 2005).

An additional aim of the present study was to examine how various potential social-environmental stressors such as home environment stress, financial stress, and racial discrimination stress are related. Exploratory correlational analyses revealed that these indices of stress were largely unrelated with the exception of household constellation, which was significantly positively correlated with financial stress. This

relationship suggests that mothers with more biological children likely have more expenses, thus, increasing the likelihood of financial strain marked by considerable unmet material need and an inability to make ends meet. Although only approaching significance, it is important to note that the relationship between financial stress and home chaos and home routine were in the expected direction such that greater financial stress may be related to more disorder and less structure in the mothers' home environments. This corresponds to past research demonstrating that individuals from low-income families and households experience higher levels of home chaos than those from wealthier families (Evans et al., 2005).

For the third hypothesis, maternal psychological distress, as measured by mothers' reports of depressive symptoms on the CES-D, was significantly positively correlated with both racial discrimination stress and financial stress, but not stressors related to the home environment. There is extensive research providing evidence that racism is a considerable stressor for many African Americans and that exposure to racism is related to a number of adverse outcomes, including poor physical and mental health (Jackson et al., 1995; Paradies, 2006; Williams, 1995). In a closer examination of racism as a cause of depression, Fernando (1984) suggested a social model of depression in this vulnerable population, positing that racism lowers self-esteem, creates feelings of loss, and contributes to feelings of learned helplessness. Regarding financial stress, research has shown that low income is correlated with higher psychiatric morbidity including higher odds of persisting depression (Lorant et al., 2003). Thus, the findings from the present study support existing research on the relationship between financial hardship,

racial discrimination, and depression, particularly in the context of mothers of children with SCD.

The hypothesis that higher levels of social-environmental stress would be associated with lower levels of positive parenting was partially supported. Positive maternal parenting was significantly positively correlated with home routine, but was not related to home chaos or household constellation. Furthermore, positive parenting shared a significant negative relationship with financial stress, such that mothers with higher levels of financial strain reported fewer positive parenting behaviors, including child monitoring and consistent discipline, with their children with SCD. Although the present study focused on positive parenting rather than negative parenting, these results are consistent with findings that parents with lower incomes are more likely to exhibit negative parenting behaviors that are generally less nurturing and less responsive. Additionally, these parents are less likely to engage in positive parent-child interactions (Guo & Harris, 2000; Hart & Risely, 1995). These results are based on mothers' self-reports of their own parenting behaviors, which are likely susceptible to the problem of shared method variance by relying on the same method to measure both constructs. Thus, it is possible that a stronger test of the relationship between maternal social-environmental stress and parenting behaviors, both negative and positive, can be obtained when parent-child interactions are observed directly.

After determining the magnitude and direction of the relationships between mothers' social-environmental stress, psychological distress and positive parenting behaviors, I examined their independent associations with several domains of cognitive functioning in their children with sickle cell disease. Maternal home environment stress

(i.e., household constellation, home chaos and home routine) was generally unrelated to cognitive function in children, with the exception of home routine, which was negatively associated with executive function problems. Mothers' racial discrimination stress was also largely unrelated to cognitive function outcomes in children with SCD. However, it is possible that mothers' personal experiences with racial discrimination are internalized and have little or no bearing on children's cognitive development either directly or indirectly through parenting behaviors. Alternatively, levels of these types of stress may not have been sufficiently high to have effects on parenting and children's cognitive function.

Although several indicators of social-environmental stress were not related to children's cognitive function, higher levels of maternal financial stress were linked to lower cognitive function across all domains. Specifically, greater financial stress was associated with poorer verbal intelligence, full-scale intelligence and academic achievement and more executive function problems. Additionally, maternal depression was linked to both academic achievement and executive function, but was not significantly related to children's scores on any of the three intelligence indices. Finally, mothers' positive parenting behaviors were not related to their children's intellectual ability or school achievement but shared a significant negative relationship with executive dysfunction, such that mothers who reported engaging in more positive parenting behaviors also reported fewer executive function problems in their children with SCD.

A series of linear regression analyses were conducted in an effort to better understand the relative influence of each of the previously discussed maternal factors on

cognitive function in pediatric SCD patients. Based on previous research suggesting that parenting may mediate the relationship between poverty and children's cognitive functioning (e.g., Evans, Boxhill & Pinkava, 2008; Evans et al., 2010), I anticipated that these analyses would demonstrate the unique role of maternal parenting in accounting for cognitive differences in this sample. The exploration generated several important findings. First, there were differences in the degree to which maternal factors account for variance in performance intelligence and verbal intelligence. Second, maternal depression and positive parenting were significant predictors of children's executive function, but not intelligence or achievement. Third, financial stress appears to be the strongest and most consistent predictor across all domains of cognitive function in the present sample of children with sickle cell disease. The rationale and implications of each of these findings are discussed in greater detail.

Differences in performance and verbal intelligence. Children's performance IQ and verbal IQ scores were entered as dependent variables in two separate linear regression analyses to better understand their relationships to maternal social-environmental stress. While none of the maternal factors served as significant predictors of children's performance IQ, maternal financial stress accounted for a significant amount of variance in several models predicting verbal intelligence. This suggests that mothers' financial situations are distinctly related to pediatric SCD patients' verbal comprehension within the larger sphere of intellectual ability. Unfortunately, few studies have concurrently examined the differential relationships between income or SES and children's verbal and performance (or non-verbal) intelligence. However, there is a large body of research that has established a link between family income (and other indicators

of SES) and language development in children (e.g., Arriaga, Fenson, Cronan & Pethick, 1998; Huttenlocher, Vasilyeva, Cymerman & Levine, 2002). Given that financial hardship has major implications for a family's social environment and that language is developed in a social context, it is plausible that maternal financial stress would account for greater variance in verbal ability than non-verbal ability.

Depression and parenting as predictors of executive function. Maternal depression and positive parenting were significant predictors in the final regression model predicting executive function problems in children with SCD. This appears to be unique to the domain of executive function as these two maternal factors did not account for considerable variance in regression models predicting intelligence or academic achievement. However, this is likely due to a methodological issue. Given that child executive function, maternal depression, and maternal positive parenting behavior were all assessed based on mothers' self-reports and are all significantly correlated, it is possible that shared method variance among maternal depression and parenting amplified each variable's ability to independently predict executive function problems in pediatric SCD patients. This highlights the importance of adopting a multi-method approach (i.e., self-report of depressive symptoms, direct observation of parenting, direct testing of cognitive function) in assessing these constructs.

The importance of maternal financial stress. Across all domains of cognition in children with sickle cell disease, maternal financial stress emerged as the most consistent social-environmental predictor of functioning, accounting for significant amounts of variance in full-scale and verbal intelligence, academic achievement, and executive function. Importantly, financial strain accounted for differences in cognitive function

above and beyond positive parenting behaviors. This finding was unexpected given previous findings demonstrating that parenting may mediate the relationship between low income and cognitive function in children.

One possible explanation for this inconsistency is that mothers of children with sickle cell disease may have particularly complex financial situations that may not have been captured in prior research with non-SCD family samples. The literature on psychosocial functioning in families with chronically ill children shows that these parents are exposed to a number of stressors including financial strain (Brown et al., 2008). In particular, parents of ill children are constantly faced with the economic costs of their child's illness, which typically include medications, hospital stays, and wages lost in missed work to care for the child. This can create an overwhelming load for mothers of children with SCD who, as shown above, are already significantly more likely to experience financial hardship independent of their child's disease (Barbarin, Whitten, Bond & Conner-Warren, 1999a).

Additionally, it is possible that the measure of financial stress used in the present study is more comprehensive and sensitive in its assessment of mothers' financial stress, thus amplifying its role as a predictor of cognitive function in children with SCD. Most studies use parent income, parent education or other indicators of socioeconomic status to assess economic hardship. In the present study, however, mothers' ability to provide essential resources for their families was considered in combination with monthly income to measure financial stress. This may be an important distinction as it captures greater detail about mothers' financial situations than income alone. Indeed, research with children with SCD and their families that considers subjective and objective

measurements of poverty as separate entities shows that financial need, but not reported income, is consistently related to adjustment problems in this population (Barbarin, Whitten, Bond & Conner-Warren, 1999b). The authors highlight the broader importance of this finding, suggesting that SES indices alone may not be sufficient measures of financial distress.

Although mothers' reports of their parenting behaviors did not emerge as a significant predictor of performance in most domains of cognitive function in the present study, the implications of parenting in the development of interventions are critical and should be explored further. As mentioned above, it may be that other maternal factors, such as financial stress, were assessed using highly sensitive measures that masked the potential impact of positive parenting. If this is the case, future work may benefit from a more direct and comprehensive assessment of parenting behaviors that captures a level of detail not typically gathered from parents' self-reports. One approach would be to code specific parenting behaviors during observed parent-child interactions. Aspland and Gardner (2003) encourage the use of observational measures in assessing parenting behavior, claiming that these methods are more closely aligned with real-world processes and are less vulnerable to participant biases. Additionally, an observational approach relies exclusively on researchers' evaluations independent of parents' personal perceptions and beliefs. Further, specific aspects of responsive parenting, including scaffolding and stimulating children's thinking skills, may not have been captured by the parenting measure used in the current study.

There are other limitations to the present study that may guide developments in future research. First, 46% of the original sample failed to return for the follow-up

assessment. Of the remaining 54%, several participants failed to complete certain key instruments in the battery. The small sample size at follow-up considerably reduces the statistical power necessary to detect changes in cognitive function over time. Second, the sample is restricted in variance in SCD characteristics, as less than 5% of the children in the present study had experienced a silent stroke and none of the participants had a history of overt stroke. The literature has established that pediatric SCD patients with a history of stroke, particularly overt stroke, are at the greatest risk for cognitive impairment (e.g., Schatz & McClellan, 2006). As these cases were underrepresented in the present study, the results likely capture the higher-functioning end of cognitive impairment, rather than a wide range of abilities. Thus, in order to generalize these findings to the broader sickle cell population, future studies should, when possible, recruit a larger sample with a wider range of disease severity.

Further, the present study did not include a control group and instead compared sample means to normative data from the cognitive function measures. Normative data is generally obtained from large, representative samples from a wider population. However, the demographic characteristics of these samples may not sufficiently match those of children with SCD who are disproportionately poor and of minority status. An alternative, and perhaps stronger, approach would be to include a control group of demographically-matched, healthy children. Finally, disease-related risk factors for cognitive impairment in children with SCD (e.g., stroke, cerebral blood flow velocity, disordered breathing, etc.) were not included in the above analyses. Given the central stance that social-environmental factors may account for an additional portion of variance in children's cognitive function, it is crucial to consider the two domains concurrently.

In summary, the results of the present study partially replicate findings from past research, reaffirming that children with sickle cell disease are at risk for significant cognitive impairment across multiple domains when compared to their same-age peers. Additionally, this work extends previous findings with non-SCD children and families to show that mothers of pediatric SCD patients experience a number of social-environmental stressors, many of which are linked not only to their own depressive symptoms and parenting behaviors, but also to their children's cognitive functioning. When considered collectively, mothers' financial stress emerges as the strongest and most consistent predictor of cognitive function, which may reflect the overwhelming difficulty of raising a chronically ill child in a low-income, highly chaotic home environment. Future work with a revised methodology is necessary to better understand the complex dynamic of social-environmental stress, parenting and cognitive function in this population, with the long-term goal of identifying concrete, teachable skills that may improve functioning in children with sickle cell disease and their families.

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TABLES

Table 1. *Demographic Characteristics of Children with Sickle Cell Disease*

	M	***SD***
Age	11.23	3.21
Hospital admissions	1.75	2.42
School days missed	24.37	22.07
	N	***%***
Sickle cell type		
HbSS	34	54.0
HbSC	16	25.4
$HbS\beta^{+}$	2	3.2
$HbS\beta^{0}$	11	17.5
Presence of infarct		
No known infarct	60	95.2
Silent infarct	3	4.8
IEP in place		
No	42	73.7
Yes	15	26.3
504 plan in place		
No	49	86.0
Yes	8	14.0
Repeated grade		
No	43	74.1
Yes	15	25.9

Note. IEP: Individualized Education Program.

Table 2. *Demographic Characteristics of Mothers of Children with SCD*

	M	***SD***
Age	37.71	6.46
Monthly income	2051.33	995.34
Number of biological children	2.25	0.91
Size of household	3.98	1.41
	N	***%***
Education level		
Some high school	4	8.00
Completed high school or GED	6	12.00
Some college or trade school	28	56.00
Completed Bachelor's degree	6	12.00
Some graduate training	6	12.00
Employment status		
Not employed	6	11.80
Employed inside the home	1	2.00
Employed outside the home	42	82.40
Employed inside and outside the home	2	3.90

Table 3. *Means, Standard Deviations and One Sample t-tests Comparing Children's Performance on Cognitive Function Measures to Normative Samples.*

Measure	***M***	***SD***	***t***
WASI			
Verbal IQ	94.97	15.63	-2.47***
Performance IQ	90.73	14.29	-4.98*
Full Scale IQ	92.31	14.73	-4.01***
WJ III			
Letter-Word Identification	47.28	10.46	-1.98*
Reading Fluency	43.58	8.13	-5.74***
Calculations	46.05	10.15	-2.91**
Math Fluency	40.81	8.96	-7.53***
Spelling	48.74	10.95	-0.88
BRIEF			
Inhibit	51.07	10.36	0.79
Shift	51.54	10.50	1.13
Emotional Control	52.10	10.76	1.50
Behavioral Regulation (BRI)	51.78	10.83	1.26
Initiate	53.68	8.68	3.25**
Working Memory	57.54	10.89	5.32***
Plan/Organize	55.40	10.47	3.99***
Organization of Materials	49.46	8.23	-0.51
Monitor	52.00	10.51	1.46
Metacognition Index (MI)	55.56	10.49	4.07***
Global Executive Composite (GEC)	53.88	10.46	2.85**
DKEFS			
Verbal Fluency – Letter Fluency	48.68	9.87	-0.82
Verbal Fluency – Category Fluency	48.82	10.87	-0.67
Verbal Fluency – Category Switching	49.79	10.59	-0.12
Verbal Fluency – Switching Accuracy	52.42	10.46	1.43
Trails – Visual Scanning	44.89	11.48	-2.74**
Trails – Sequencing	48.99	10.75	-0.58
Trails – Number/Letter Switching	41.24	13.76	-3.93***
Trails – Motor Speed	49.68	9.50	-0.21
Color/Word – Word Reading	46.92	10.24	-1.85†
Color/Word – Color Naming	47.76	11.09	-1.24
Color/Word – Inhibition	44.97	10.96	-2.83**
Color/Word – Inhibition Switching	43.82	10.46	-3.65***
Confirmed Correct Card Sorts	47.89	9.05	-1.44

Note. WASI: Wechsler Abbreviated Scale of Intelligence. WJ III: Woodcock-Johnson III Tests of Achievement. BRIEF: Behavior Rating Inventory of Executive Function. DKEFS: Delis-Kaplan Executive Function System.
† p <.10. *p <.05. **p <.01. ***p <.001.

Table 4. *Correlations of Variables Considered for Data Reduction of Academic Achievement Variable.*

WJ III Test	1	2	3	4
1. Letter-Word Identification	--			
2. Reading Fluency	.71***	--		
3. Calculations	.62***	.56***	--	
4. Math Fluency	.52***	.65***	.63***	--
5. Spelling	.82***	.71***	.61***	.59***

Note. WJ III: Woodcock-Johnson III Tests of Achievement.

***p <.001.

Table 5. *Correlations of Variables Considered for Data Reduction of Household Constellation Variable.*

Household Constellation Variable	**1**	**2**	**3**	**4**	**5**	**6**
1. No. of moves in past five years	--					
2. No. of adults in home	.03	--				
3. No. of children in home	.13	.32*	--			
4. No. of biological children	.18	.20	.92***	--		
5. No. of people in home	.11	.73***	.88***	.77***	--	
6. Home routine	.01	-.12	-.08	-.04	-.12	--
7. Home chaos	-.27†	-.16	-.08	-.03	-.14	-.17

† p <.10. *p <.05. ***p <.001.

Table 6. *Correlations of Variables Considered for Data Reduction of Financial Stress Variable.*

Financial Stress Variable	**1**	**2**	**3**
1. Number of jobs	--		
2. Monthly income	.40**	--	
3. Cannot make ends meet	-.22	-.45***	--
4. Unmet material needs	-.18	-.44***	.80***

**p <.01. ***p <.001.

Table 7. *Bivariate Correlations of Children's Cognitive Function Measures, Maternal Stress and Distress, and Maternal Parenting at Baseline.*

	1	2	3	4	5	6	7	8	9	10	11
Child Cognitive Function											
1. Verbal IQ	--										
2. Performance IQ	.57***	--									
3. Full Scale IQ	.91***	.87***	--								
4. Academic Achievement	.73***	.60***	.75***	--							
5. Executive Function	-.18	-.18	-.19†	-.31*	--						
Maternal Stress and Distress											
6. Household Constellation	-.05	.07	.01	-.06	-.03	--					
7. Home Chaos	.04	-.01	.03	-.08	-.01	-.04	--				
8. Home Routine	-.01	.06	.02	.20	-.28*	-.03	-.17	--			
9. Financial Stress	-.35**	-.16	-.29*	-.36**	.34*	.30*	.27†	-.24†	--		
10. Racial Discrimination	-.05	.16	.05	-.22†	.03	.23†	-.06	-.08	.19	--	
11. Depression	-.24†	-.09	-.18	-.28*	.56***	.27†	.16	-.19	.68***	.38**	--
Maternal Parenting											
12. Positive Parenting	.07	.12	.10	.10	-.54***	-.14	-.20	.36**	-.32*	.09	-.46***

† p <.10. *p <.05. **p <.01. ***p <.001.

Table 8. *Summary of Linear Regression Analysis for Variables Predicting Child's Full Scale IQ.*

Variable	**β**	***t***	***ΔR²***
Step 1 (R^2 = .067)			0.067†
Financial Stress	-0.26	-1.83†	
Step 2 (R^2 = .078)			0.012
Financial Stress	-0.29	-1.96†	
Household Constellation	0.11	0.76	
Step 3 (R^2 = .083)			0.005
Financial Stress	-0.30	-2.00*	
Household Constellation	0.10	0.64	
Racial Discrimination Stress	0.07	0.48	
Step 4 (R^2 = .085)			0.002
Financial Stress	-0.26	-1.30	
Household Constellation	0.10	0.65	
Racial Discrimination Stress	0.09	0.55	
Maternal Depression	-0.07	-0.34	
Step 5 (R^2 = .091)			0.006
Financial Stress	-0.25	-1.23	
Household Constellation	0.10	0.64	
Racial Discrimination Stress	0.11	0.67	
Maternal Depression	-0.13	-0.54	
Positive Parenting	-0.90	-0.52	

† p <.10. *p <.05.

Table 9. *Summary of Linear Regression Analysis for Variables Predicting Child's Performance IQ.*

Variable	**β**	***t***	***ΔR²***
Step 1 (R^2 = .021)			0.021
Financial Stress	-0.14	-1.00	
Step 2 (R^2 = .035)			0.014
Financial Stress	-0.18	-1.17	
Household Constellation	0.12	0.81	
Step 3 (R^2 = .059)			0.025
Financial Stress	-0.20	-1.34	
Household Constellation	0.09	0.56	
Racial Discrimination Stress	0.17	1.08	
Step 4 (R^2 = .062)			0.003
Financial Stress	-0.16	-0.78	
Household Constellation	0.09	0.58	
Racial Discrimination Stress	0.18	1.14	
Maternal Depression	-0.08	-0.37	
Step 5 (R^2 = .062)			0.000
Financial Stress	-0.16	-0.77	
Household Constellation	0.09	0.57	
Racial Discrimination Stress	0.18	1.09	
Maternal Depression	-0.08	-0.34	
Positive Parenting	-0.01	-0.03	

Table 10. *Summary of Linear Regression Analysis for Variables Predicting Child's Verbal IQ.*

Variable	**β**	***t***	***ΔR²***
Step 1 (R^2 = .100)			0.100*
Financial Stress	-0.32	-2.29*	
Step 2 (R^2 = .107)			0.007
Financial Stress	-0.34	-2.35*	
Household Constellation	0.09	0.60	
Step 3 (R^2 = .107)			0.000
Financial Stress	-0.34	-2.27*	
Household Constellation	0.09	0.60	
Racial Discrimination Stress	-0.02	-0.12	
Step 4 (R^2 = .109)			0.002
Financial Stress	-0.30	-1.54†	
Household Constellation	0.09	0.62	
Racial Discrimination Stress	-0.004	-0.03	
Maternal Depression	-0.06	-.29	
Step 5 (R^2 = .121)			0.012
Financial Stress	-0.28	-1.44	
Household Constellation	0.09	0.61	
Racial Discrimination Stress	0.03	0.18	
Maternal Depression	-0.14	-0.62	
Positive Parenting	-0.13	-0.77	

† p <.10. *p <.05.

Table 11. *Summary of Linear Regression Analysis for Variables Predicting Child's Academic Achievement.*

Variable	**β**	***t***	***ΔR²***
Step 1 (R^2 = .112)			0.112*
Financial Stress	-0.34	-2.41*	
Step 2 (R^2 = .114)			0.002
Financial Stress	-0.35	-2.40*	
Household Constellation	0.05	0.33	
Step 3 (R^2 = .153)			0.039
Financial Stress	-0.31	-2.13*	
Household Constellation	0.09	0.65	
Racial Discrimination Stress	-0.21	-1.41	
Step 4 (R^2 = .153)			0.000
Financial Stress	-0.29	-1.54†	
Household Constellation	0.10	0.64	
Racial Discrimination Stress	-0.20	-1.28	
Maternal Depression	-0.03	-0.15	
Step 5 (R^2 = .155)			0.002
Financial Stress	-0.29	-1.48	
Household Constellation	0.09	0.63	
Racial Discrimination Stress	-0.19	-1.13	
Maternal Depression	-0.06	-0.28	
Positive Parenting	-0.05	-0.32	

† p <.10. *p <.05.

Table 12. *Summary of Linear Regression Analysis for Variables Predicting Child's Executive Function as Measured by the BRIEF.*

Variable	**β**	***t***	***ΔR²***
Step 1 (R^2 = .146)			0.146**
Financial Stress	0.38	2.84**	
Step 2 (R^2 = .152)			0.006
Financial Stress	0.40	2.86**	
Household Constellation	-0.08	-0.55	
Step 3 (R^2 = .152)			0.000
Financial Stress	0.40	2.80**	
Household Constellation	-0.07	-0.51	
Racial Discrimination Stress	0.01	0.09	
Step 4 (R^2 = .355)			0.203***
Financial Stress	0.01	0.06	
Household Constellation	-0.11	-0.82	
Racial Discrimination Stress	-0.16	-1.21	
Maternal Depression	0.65	3.72***	
Step 5 (R^2 = .415)			0.061*
Financial Stress	0.04	0.28	
Household Constellation	-0.11	-0.86	
Racial Discrimination Stress	-0.08	-0.63	
Maternal Depression	0.46	2.45*	
Positive Parenting	-0.29	-2.12*	

*p <.05. **p <.01. ***p <.001.

Table 13. *Means, Standard Deviations and Paired Samples t-tests Comparing Children's Performance on Cognitive Function Measures at Time 1 and Time 2.*

	Time 1		Time 2		
Measure	***M***	***SD***	***M***	***SD***	***t***
WASI (N = 38)					
Verbal IQ	94.66	15.49	93.21	13.28	1.12
Performance IQ	91.63	14.20	92.63	12.31	-0.58
Full Scale IQ	92.45	14.30	92.32	12.90	0.13
WJ III (N = 37)					
Letter-Word Identification	48.86	8.73	45.68	8.73	3.16**
Reading Fluency	44.41	7.35	43.74	7.96	0.68
Calculations	46.22	10.70	43.83	10.35	1.70†
Math Fluency	41.06	8.75	39.74	10.71	1.19
Spelling	49.97	9.40	47.05	8.39	3.54***
BRIEF (N = 39)					
Inhibit	50.23	10.21	49.15	8.25	0.88
Shift	51.31	10.68	48.72	8.20	1.43
Emotional Control	52.79	11.46	49.53	9.55	2.02*
Behavioral Regulation (BRI)	51.74	49.08	11.25	8.49	1.75†
Initiate	53.59	8.71	50.36	6.86	2.77**
Working Memory	57.74	10.95	55.18	9.49	1.65
Plan/Organize	55.24	10.49	52.97	8.33	1.44
Organization of Materials	49.36	9.06	48.41	7.29	0.91
Monitor	52.72	11.28	50.13	9.50	1.84†
Metacognition Index (MI)	55.55	11.23	52.26	7.32	2.05*
Global Executive Composite (GEC)	53.92	10.94	52.68	10.34	0.74
DKEFS (N = 21)					
Verbal Fluency – Letter Fluency	48.38	8.46	47.29	6.70	0.74
Verbal Fluency – Category Fluency	48.86	11.49	46.14	10.59	1.33
Verbal Fluency – Category Switching	51.29	11.39	49.10	8.35	0.92
Verbal Fluency – Switching Accuracy	52.10	10.43	55.90	10.38	-1.62†
Trails – Visual Scanning	48.10	10.01	39.75	12.35	2.44*
Trails – Sequencing	48.02	11.37	49.67	10.81	-0.65
Trails – Number/Letter Switching	40.86	13.40	43.24	14.25	-0.89
Trails – Motor Speed	48.10	11.10	51.19	9.07	-1.89†
Color/Word – Word Reading	45.62	10.05	45.81	10.48	0.09
Color/Word – Color Naming	47.10	11.51	46.90	10.53	-0.08
Color/Word – Inhibition	45.86	10.43	42.43	12.95	1.86†
Color/Word – Inhibition Switching	44.20	11.08	45.60	10.99	-0.47

Confirmed Correct Card Sorts	48.29	9.45	47.62	7.61	0.28

Note. WASI: Wechsler Abbreviated Scale of Intelligence. WJ III: Woodcock-Johnson III Tests of Achievement. BRIEF: Behavior Rating Inventory of Executive Function. DKEFS: Delis-Kaplan Executive Function System.

† p <.10. *p <.05. **p <.01. ***p <.001.