Neuropsychological Functioning of Youths With Sickle Cell Disease: Comparison With Non-Chronically Ill Peers

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Objective: To compare the neuropsychological functioning of children with sickle cell disease (SCD) with no evidence of overt clinical stroke to that of classmates without a chronic illness matched on gender, race, and age. We examined both overall level of performance and patterns of performance utilizing empirically derived construct scores of key domains of neurocognitive functioning.

Methods: An abbreviated neuropsychological battery of tests was given to 31 children with SCD and 31 case controls. Empirically derived construct scores were developed for primary analyses.

Results: Children with SCD had significantly lower scores on three level-of-performance construct scores: total, verbal, and attention/memory. Mean scores for children with SCD were lower than those for case controls on every level-of-performance construct score and every standardized test score. However, pattern-of-performance construct scores were not significantly different.

Conclusions: Children with SCD without overt stroke demonstrate significant deficits in neurocognitive functioning compared to classroom case controls. These findings highlight the impact of SCD on general neurocognitive functioning and suggest that routine screening of cognitive functioning should be a requisite element of comprehensive care for children with SCD. Within the context of documented physical limitations, we conclude that children with SCD are at very high risk for impaired psychosocial outcomes.

Key words: sickle cell disease; neuropsychology; children.

Sickle cell disease (SCD) is a collective term for a group of genetic disorders characterized by the predominance of hemoglobin S (Hgb S), an abnormal type of hemoglobin (Hgb). SCD occurs primarily in persons of African, Mediterranean, Indian, and Middle Eastern heritage (Charache, Lubin, & Reid, 1992). In the United States, it is found predominantly, but not exclusively, in the African American population (Lin-Fu, 1972). The two main pathophysiological features of SCD are chronic hemolytic anemia (premature destruction of red blood cells) and vaso-occlusion (blockage in the blood vessels) (Charache et al., 1992; Cotran, Kumar, & Robbins, 1989). Both of these aberrant processes can cause central nervous system (CNS) damage associated with denigration of cognitive functioning. Chronic hemolytic anemia can result in hypoxia because of
the shortage of red blood cells to supply oxygen to the brain. Vaso-occlusion can lead to strokes.

Although overt stroke is an obvious cause of neurologic abnormality and cognitive impairment, information about the cognitive functioning of children with SCD who have not had an overt stroke is contradictory. Early research suggested that no cognitive impairments were associated with SCD (Chodorkoff & Whitten, 1963). Using more comprehensive measurement strategies and improved designs, more recent studies examining children with SCD with no evidence of overt stroke have generally reported deficits in neurocognitive functioning. However, findings across studies are inconsistent (Table I). Two studies reported lower overall intelligence test scores (Swift et al., 1989; Wasserman, Wilimas, Fairclough, Mulhern, & Wang, 1991), and three have reported lower scores on standardized academic achievement tests, especially in reading (Brown, Buchanan, et al., 1993; Fowler et al., 1988; Swift et al., 1989). One study reported spatial/constructional deficits (Fowler et al., 1988). Three studies reported attention/memory deficits (Brown, Buchanan, et al., 1993; Fowler et al., 1988; Swift et al., 1989). In contrast, three studies reported no significant findings on overall intelligence (Brown, Buchanan, et al., 1993; Fowler et al., 1988; Goonan, Goonan, Brown, Buchanan, & Eckman, 1994); two studies reported no differences between children with SCD and comparison children on academic achievement (Richard & Burlew, 1997; Wasserman et al., 1991); one study found no differences on spatial/constructional abilities (Swift et al., 1989); and one study found no differences on measures of sustained attention and inhibitory control (Goonan et al., 1994). Although several of these investigators examined the role of variables that could moderate or mediate (Baron & Kenny, 1986) the relationship between SCD and neurocognitive functioning (i.e., disease severity or school absenteeism), findings have not been supportive (e.g., Goonan et al., 1994).

Because SCD is a life-long condition, age effects have also been examined. Again, the results are not consistent. Three studies using a weak cross-sectional design (Achenbach, 1978) have reported that older children show greater neuropsychological impairment in reading achievement (Fowler et al., 1988), spatial/constructional functioning, and sustained attention (Brown, Buchanan, et al., 1993; Fowler et al., 1988). In support of the cross-sectional data, recent preliminary longitudinal findings from the Cooperative Study of Sickle Cell Disease also suggest significant declines with age (Wang et al., 1999). In contrast, Wasserman et al. (1991) reported greater deficits in younger children with SCD.

These inconsistent findings from recent studies with modest sample sizes suggest the need for further investigation about the neurocognitive functioning of children with SCD. The use of a sibling comparison group (Brown, Buchanan, et al., 1993; Goonan et al., 1994; Swift et al., 1989; Wasserman et al., 1991) ensures comparability on numerous sociodemographic and biologic factors. However, it does not allow for matching on age and gender and is limited to children with SCD who have a sibling. Previous research has suggested that chronic illness can have a deleterious effect on siblings (Sahler

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<tbody>
<tr>
<td>Sample size</td>
<td>SCD/COMP N = 28</td>
<td>SCD/SIB N = 21</td>
<td>SCD N = 43</td>
<td>SCD N = 70</td>
<td>SCD N = 42</td>
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<tr>
<td>Age range</td>
<td>6–17 yrs</td>
<td>7–16 yrs</td>
<td>8–16 yrs</td>
<td>2.5–17 yrs</td>
<td>7–11 yrs</td>
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<tr>
<td>Overall intelligence</td>
<td>No differences</td>
<td>Lower</td>
<td>No differences</td>
<td>No differences</td>
<td>—</td>
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<tr>
<td>Academic skills</td>
<td></td>
<td></td>
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<tr>
<td>Spelling</td>
<td>Lower</td>
<td>—</td>
<td>No differences</td>
<td>—</td>
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<tr>
<td>Reading</td>
<td>Lower</td>
<td>Lower</td>
<td>No differences</td>
<td>Lower</td>
<td>No differences</td>
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<tr>
<td>Mathematics</td>
<td>No differences</td>
<td>Lower</td>
<td>No differences</td>
<td>—</td>
<td>No differences</td>
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<tr>
<td>Spatial/construction</td>
<td>Lower</td>
<td>No differences</td>
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<td>Attention/memory</td>
<td>Lower</td>
<td>Lower</td>
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<td>No differences</td>
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<tr>
<td>Age effects</td>
<td>Older: greater</td>
<td>No differences</td>
<td>Younger: greater</td>
<td>Older: greater</td>
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<td>impairment</td>
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COMP = comparison children, SIB = sibling, Lower = lower scores for children with SCD, Dash = not reported.
et al., 1994), which further complicates the use of siblings for comparison of levels of functioning. Fowler et al. (1988) used a matched comparison group, but their matching procedure did not permit the use of an ex post facto design without the usual risk of spurious variables confounding the results (Meehl, 1970). Their comparison group was a volunteer sample, and they did not report recruitment rates. Finally, all of the previously reported work made a large number of comparisons with a variety of neurocognitive measures and no preplanned data reduction strategy. Recent work in developmental psychology has delineated procedures for data reduction that allow for empirical construct building (Capaldi & Patterson, 1991). Although this strategy has not been reported in child neuropsychology, this empirical approach to construct building and data reduction provides the opportunity to assess key domains systematically with multiple indicators and fewer statistical tests.

The inconsistent findings from the previous research may be an accurate reflection of the impact of “silent strokes” on neurocognitive functioning (Armstrong et al., 1996). Children with SCD have evidence of subtle cerebrovascular infarcts, in which the child does not suffer an obvious clinical episode, but brain abnormalities are evident on neuroimaging (Pavlakis et al., 1988). Armstrong et al. (1996) found that silent stroke had occurred in 12%–16% of their sample of children with SCD and that children with SCD who had evidence of silent cerebral infarcts obtained lower full-scale IQ scores. Because children with SCD can demonstrate distinctive patterns of cerebrovascular damage, one might expect that neurocognitive deficits would vary from child to child. Each study with a small sample of children subsequently reports slightly different findings. Within this context, it seems possible that children with SCD would manifest greater variability between neurocognitive domains of functioning. The research literature has paid minimal attention to systematically evaluating variability between neuropsychological domains of functioning, although this strategy is widely used clinically. One of the goals of this work was to begin to develop an empirical measurement strategy to assess neuropsychological variability so we could begin to explore whether children with SCD demonstrate greater variability between neurocognitive domains.

Our first aim was to obtain neuropsychological data for children with SCD and case controls. The case controls were classmates matched for race, gender, and age, with no chronic illness. Although previous work (Brown, Buchanan, et al., 1993) has called for the use of a classmate comparison group matched for age, gender, race, and demographics, this type of work has not yet been reported. We hypothesized that, compared to case controls, children with SCD would have lower overall cognitive functioning, lower academic achievement (especially in reading), and poorer attention/memory (hypothesis 1: main effects) and that these differences would be greater for older children with SCD (hypothesis 2: interaction). To limit the number of comparisons, we used a standard construct-building technique.

Our second aim was to develop standardized pattern of performance scores. These scores would be indicators of discrepancy in functional performance between distinct domains of neuropsychological functioning. We postulated that the effects of SCD on the CNS would cause atypical patterns of performance. We hypothesized that children with SCD would show greater variability between neurocognitive domains of functioning than case controls (hypothesis 3).

Method
Participants

Children with SCD were identified using hospital records listing all patients with SCD who had received treatment at this medical center (Noll et al., 1996). Because this facility is the only hospital with board-certified pediatric hematologists in the metropolitan area, and the only inpatient pediatric facility, nearly every patient with SCD in the catchment area is listed in the hospital records. Children with SCD were initially eligible to participate if they were between 9 and 16 years of age, had no history of overt stroke, and were not receiving full-time special education. None of the participants who were identified using hospital records had a history of overt stroke, and no one was in full-time special education, so no one was excluded on the basis of these criteria. Thirty-six children were randomly selected for this study from a larger group of 80 children with SCD who met our inclusion criteria. Thirty-one (86%) participated (two could not be located and three declined to participate). The size of our sample was restricted because of fiscal lim-
Approximately half of the children had HgbSS \((n = 15)\) or HgbSβthal \((n = 1)\), the more severe genotypes of the disease, and the remainder had either HgbSC \((n = 9)\) or HgbSβthal \((n = 6)\).

Case controls were recruited using a case-by-case matching procedure. For each child with SCD, we used a roster listing all their classmates to identify the child of the same race and gender with the closest date of birth. Parents of that child were contacted and asked to participate in this research. They were told that the goal of the research was to learn more about the impact of chronic illness on children and their families and that this work involved the participation of families of children without a chronic illness, as well as those with a chronic illness. Twenty-nine (94%) of our first-choice families agreed to participate; the other two were the second closest date of birth. There were 13 boys and 18 girls in each group. The mean group ages were 11.9 years \((SD = 1.4)\) for SCD and 11.6 years \((SD = 1.4)\) for case controls. All participants were African American.

**Parent Measures**

*Demographic Background Questionnaire* (Noll et al., 1996, 1999). This instrument assesses basic background characteristics of the adult who completes the measure. Adequate data are available to ascertain the socioeconomic status (SES) of each family with the Revised Duncan (TSEI2; Stevens & Featherman, 1981), an occupation-based measure of SES. This measure was selected as a result of work by sociologists suggesting that occupation-based measures represent a contemporary indicator of SES (Hauser, 1994; Mueller & Parcel, 1981). Information is also obtained on martial status, parental education, family income, age of respondent, and number of children living at home.

**Child Measures**

All of the neuropsychological measures used are widely available and have acceptable psychometric qualities (Sattler, 1988). They also have a history of use with children with SCD. The Wechsler Intelligence Scale for Children-Revised (WISC-R; Wechsler, 1974) was used to evaluate the child’s general intelligence. Four recent neuropsychological studies of children with SCD have used this measure. The Wide Range Achievement Test-Revised (WRAT-R; Jastak & Wilkinson, 1984) is a widely used screening test for academic achievement in three skill domains: reading, spelling, and arithmetic. Previous work with children with SCD has used this measure. The Beery Developmental Test of Visual-Motor Integration-3rd revision (VMI; Beery, 1989) evaluates the child’s spatial/constructional abilities. The Kagan Matching Familiar Figures Test (MFFT; Kagan, 1966) is designed to measure sustained attention and impulse control. The Wide Range Assessment of Memory and Learning (WRAML; Sheslow & Adams, 1990) is designed to evaluate the child’s ability to learn and memorize information. We utilized the Design Memory and Sentence Memory subtests of the WRAML because they have been shown to load the highest on the visual and verbal factors of this test. We included this measure in our battery because previous work had strongly suggested that children with SCD have memory problems (Brown, Buchanan, et al., 1993; Fowler et al., 1998; Swift et al., 1989). The Purdue Pegboard Test (Tiffin, 1948) is designed to measure fine motor speed and manual dexterity. Previous work has demonstrated the sensitivity of this measure to lateralized lesions (Costa, Vaughan, Levita, & Farber, 1963), so it was included as a sensitive measure of lateralized fine motor deficits.

**Procedures**

After obtaining informed consent from the parent and child, we administered the complete battery of neuropsychological tests to the child. Data were collected in the home for all children because the setting was more convenient for families and similar for both groups. Data collectors (i.e., doctoral students in clinical child psychology) were trained and supervised by a pediatric neuropsychologist (MDR). None of the children was taking narcotic medication for pain during the testing, and none of the children reported or appeared to be in pain during the assessment. The data collection session lasted approximately 3 hours, and families received $50 for their participation.

**Level-of-Performance Construct Development**

Our approach to construct building used multiple overt indicators of our latent variables (Capaldi & Patterson, 1991). This systematic approach to data reduction and measurement was used to evaluate key neurocognitive domains relevant to the neuropsychological functioning of children with SCD.
(verbal, spatial/constructional, attention/memory, etc.). Pediatric neuropsychological evaluations routinely employ batteries of tests aimed at discerning strengths and deficits in broadly defined domains of functioning. These batteries often include multiple indicators of a single domain of functioning. Traditionally, individual test scores have been reported in studies addressing neuropsychological functioning of children with SCD. The construct building approach is advantageous because it allows us to perform fewer analyses, minimizing Type I error, while simultaneously producing a more robust indicator of the latent variable. The construct building approach to data reduction we used has advantages over strict reliance on multivariate techniques (e.g., forming scales based on exploratory factor analysis), because it produces theory-based measures developed through a series of empirical iterative steps.

First, two pediatric psychologists (RBN and MDR) with considerable experience in neuropsychology and SCD examined the literature addressing neuropsychological functioning of children with SCD and the general pediatric neuropsychology literature, to identify key domains of neurocognitive functioning. Five domains (verbal, spatial/constructional, achievement, attention/memory, fine motor) were selected as our latent variables. Second, we selected a brief neuropsychological battery of tests that included multiple measures of each important latent variable. Third, tests or subtests were independently selected by three pediatric neuropsychologists who were not involved in this research as potential overt indicators of each of our five latent variables. We included only those tests/subtests that included multiple measures of each important latent variable. Fourth, the internal consistency of each overt indicator (subscales or tests) was evaluated using Cronbach’s α and item-total correlations. The a priori requirements were Cronbach’s α >.60 and item-total correlations >.20. Fifth, a confirmatory factor analysis was completed on each set of scales/tests making up each of the five constructs. The factor analysis was initially performed on half of the sample (randomly selected) and subsequently replicated with the other half, to ensure cross-sample stability of the factor loadings. Only indicators with factor loadings >.3 for both factor analyses were retained and subsequently included in the construct. Although there are potential problems with factor analyses using small samples, the coherent factor structure with cross-sample replication suggests robust relationships between variables. Results from these data reduction procedures are available from Dr. Gartstein.

Level-of-performance constructs were developed by summing variables associated with each of the factors. Five principal neurocognitive domains were defined according to the following formulas, developed to yield standard scores (M = 100, SD = 15; note: * = multiply):


2. Spatial/Constructional = [(5*WISC-R Picture Completion + 50) + (5*WISC-R Picture Arrangement + 50) + (5*WISC-R Block Design + 50) + (5*WISC-R Object Assembly + 50) + (5*WISC-R Mazes + 50) + VMfI]/6.

3. Achievement = (WRAT-R Reading + WRAT-R Spelling + WRAT-R Arithmetic)/3.

4. Attention/Memory = [(5*WISC-R Arithmetic + 50) + (5*WISC-R Digit Span + 50) + (5*WISC-R Coding + 50) + (5*WRAML Sentence Memory + 50) + (5*WRAML Design Memory + 50) + (1.5*MFFT Errors + 25) + ((150–1.5*MFFT Latency) + 25)]/7.

5. Fine Motor = [(1.5*Pegs Dominant Hand + 25) + (1.5*Pegs Nondominant Hand + 25) + (1.5*Pegs Both Hands + 25)]/3.

6. A Total Level-of-Performance construct score was computed by averaging the five domain construct scores.

Additional technical information regarding these constructs and their development can be obtained from Dr. Noll.

**Pattern-of-Performance Construct Development**

The pattern-of-performance scores were developed to examine empirically discrepancies between domains of neuropsychological functioning. These discrepancies often form the basis of diagnoses. For example, a nonverbal learning disability may be diagnosed on the basis of a pattern of significantly lower spatial/constructional scores compared to significantly higher verbal scores. In clinical practice, these decisions are made on the basis of profile analysis highly dependent on the clinical skill of the examiner. For this research, we used an empirical method to evaluate discrepancies between domains.
of neuropsychological functioning to test hypothesis 3.

The procedure developed for the evaluation of discrepancies included multiple steps. We will use the comparison of overall intelligence (IQ) versus overall achievement (ACH) as an example. First, the senior pediatric psychologists (MDR and RBN) selected the discrepancies they believed were most relevant on the basis of their clinical experiences with children who have SCD. Second, for each pair of neurocognitive domains, we performed regression analyses to determine the extent to which one neurocognitive variable (ACH) could be predicted on the basis of the second neurocognitive variable (IQ). This regression procedure generated a set of equations, which could be used to compute predicted scores. These predicted scores (e.g., predicted ACH) represent the element of the dependent variable (ACH) that is consistent or correlated with the independent variable (IQ). In statistical terms, a predicted score represents the variance of the dependent variable (ACH) that is common with the independent variable (IQ). The differences between the predicted (e.g., ACH predicted on the basis of IQ) and observed scores (actual ACH) represent the discrepancies between the different domains. Greater differences represent more significant discrepancies. Discrepancy scores represent the standardized differences between two domains of neuropsychological functioning.

Pattern-of-performance construct scores were developed to represent the degree of variability in a participant’s performance across six different pairs of neuropsychological scores: (1) overall achievement versus overall IQ, (2) overall memory versus overall IQ, (3) overall memory versus overall achievement, (4) performance IQ versus verbal IQ, (5) pegs dominant versus pegs nondominant, (6) sentence memory versus design memory, and (7) a total pattern-of-performance score computed by averaging the six discrepancy scores. The overall memory construct was computed using the WRAML Sentence Memory and Design Memory scores.

**Data Analysis**

Thirteen 2 × 2 mixed factorial ANOVAs were conducted for the six level-of-performance and seven pattern-of-performance construct scores. Type of child (SCD or case control) was a within-participants variable and age was a between-participants variable (based on a median split at 11.42 years). All analyses were completed using construct scores based on standard scores. Raw score variability across subtests prohibited their use in the development of constructs. To reduce the probability of Type I error (except for demographics), Holm’s procedure was used (Holland & Copenhaver, 1989), an improved Bonferroni procedure. All significant results remained significant after our adjustment for multiple comparisons except one (MFFT error), although the p values presented in the tables are not adjusted for multiple comparisons. To facilitate subsequent comparisons with already published data and future studies, we present standard score findings for all neuropsychological measures in our battery, although primary analyses were conducted with the 13 construct scores.

**Results**

**Demographics**

The background characteristics of the families of children with SCD and case controls were compared using t tests (Table II). Analyses revealed no significant differences between the two groups in family

<table>
<thead>
<tr>
<th>Variable</th>
<th>SCD</th>
<th>SD</th>
<th>Case Control</th>
<th>SD</th>
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<tbody>
<tr>
<td>Family social prestigea</td>
<td>23.7</td>
<td>13.6</td>
<td>25.9</td>
<td>17.9</td>
<td>0.65</td>
</tr>
<tr>
<td>Gross family incomeb</td>
<td>14.5</td>
<td>12.2</td>
<td>17.7</td>
<td>19.6</td>
<td>1.03</td>
</tr>
<tr>
<td>Income per personc</td>
<td>4.1</td>
<td>3.0</td>
<td>5.1</td>
<td>6.0</td>
<td>0.99</td>
</tr>
<tr>
<td>Number of children in the home</td>
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<td>1.5</td>
<td>2.7</td>
<td>1.1</td>
<td>0.09</td>
</tr>
<tr>
<td>Age of primary caregiver</td>
<td>36.9</td>
<td>6.6</td>
<td>38.5</td>
<td>5.7</td>
<td>1.13</td>
</tr>
<tr>
<td>Years of education of primary caregiver</td>
<td>12.4</td>
<td>1.5</td>
<td>13.0</td>
<td>2.2</td>
<td>1.13</td>
</tr>
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</table>

# Table II. Demographic Features of Families with a Child Who Has SCD (n = 31) and Case Control Families (n = 31)

- Revised Duncan Sociometric Index (TSEI2; Stevens & Featherman, 1981), a widely used indicator of occupation ranking.
- In thousands of dollars.
- This represents the average income per person living in the household supported by the family’s gross income, in thousands of dollars.
social prestige, gross family income, income per person, number of children in the home, age of the primary caregiver, or years of education of the primary caregiver. The family social prestige scores suggest that the primary caregivers had occupational roles predominantly in clerical, service, and semi-skilled laborer positions.

**Neuropsychological Data Analyses**

*Level-of-Performance Scores.* A significant main effect for type of child was indicated for three of our level-of-performance scores (verbal, attention/memory, and total; Table III). Additionally, for every comparison, the children with SCD scored lower than case controls. There were no significant interactions with age using age as a continuous variable in multiple regressions or using age as a factor score in a median-split ANOVA procedure.

Additional supplementary analyses were performed on WISC-R, WRAT-R, VMI, WRAML, MFFT, and Purdue Pegboard (Table III). These are labeled supplementary because we conducted our primary analyses on the empirically developed constructs. Children with SCD had significantly lower verbal IQ and full-scale IQ. Scores were also significantly different on the MFFT latency score and WRAT-R arithmetic. Differences were not significant for the WRAT-R reading and spelling, VMI, WRAML, MFFT error (after Holm’s correction), or the pegboard scores, although children with SCD scored lower than controls on each of these tests. There were no significant interactions with age (Table III). These analyses provide support for hypothesis 1 but do not support hypothesis 2.

*Pattern-of-performance Scores.* Comparisons of the six discrepancy constructs and the total pattern-of-performance discrepancy score between children with SCD and case controls showed no significant main effects or interactions (Table III). These findings do not support hypothesis 3, which suggested that children with SCD have greater variability in neurocognitive functioning.

**Discussion**

This study examined the neuropsychological functioning of youths with SCD who had no history of overt CNS disease and case controls. These findings support recent research suggesting that youths with SCD are vulnerable to increased difficulties in several domains of neuropsychological functioning (Brown, Buchanan, et al., 1993; Fowler et al., 1988; Swift et al., 1989; Wasserman et al., 1991). We had hypothesized that children with SCD would show lower overall cognitive functioning, attention/memory, and achievement (especially in reading), with deficits more pronounced for older children with SCD. The performance of children with SCD was significantly lower than that of case controls on three of our level-of-performance scores (verbal, attention/memory, and total). Follow-up supple-
mentary analyses using scores from the individual neurocognitive measures included in this study showed a similar pattern of difficulties. Of note, scores of children with SCD were lower than those of case controls on every measure of functioning. Cross-sectional analyses examining the interaction between age and SCD showed no significant interactional effects for age when evaluated categorically in an ANOVA model (based on a median split) or as a continuous variable in a multiple regression procedure. These data suggest cognitive risk for children with SCD (hypothesis 1) but do not support hypothesis 2.

To test hypothesis 3, we developed pattern-of-performance scores. All comparisons with case controls using these indicators were nonsignificant. Within the context of our general findings of deficits, these data suggest that children with SCD are susceptible to general deficits in cognitive functioning but do not demonstrate greater variability between selected domains.

Because silent strokes are thought to cause neurocognitive variability, our generalized findings suggest that hypoxia (i.e., chronic anemia, sleep hypoxia, poor pulmonary functioning, etc.) may play a role in the pathophysiology of problems (Brown, Buchanan, et al., 1993). This conjecture is made because deficits were significant across several domains and children with SCD obtained lower scores across all measured domains. Alternatively, silent strokes may have a more generalized impact on neurocognitive functioning for children with SCD who have not had an overt stroke. From this perspective, subtle and progressive large and small vessel disease eventually is associated with a stroke but also causes disruption of neural processes even before a stroke occurs. Future work might begin to examine physiological indices of hypoxia to determine whether supporting evidence can be obtained. Of note, a life-long chronic illness alone may cause neurocognitive difficulties as a result of excessive absenteeism from school and chronic fatigue that limits a child's enthusiasm for academics.

Because our research is the first to examine empirically whether children with SCD demonstrate greater variability in cognitive functioning, and we examined only a limited number of patterns, additional research examining variability of neuropsychological functioning is needed. This work might use the design employed in this study (case control classmates or nonafflicted siblings) across multiple sites to increase sample size and could focus on assessment of discrepancies between indicators of neurocognitive functioning.

Previous researchers who examined attention and concentration also found that youths with SCD had deficits in these two domains (Brown, Buchanan, et al., 1993; Fowler et al., 1988; Swift et al., 1989). Difficulties with attention and concentration have also been reported by researchers examining behavior of children with SCD (Brown, Kaslow, et al., 1993; Hurtig & Park, 1989; Hurtig & White, 1986), although Goonan et al. (1994) did not find problems with sustained attention and inhibitory control. Although it is unclear why this specific domain of functioning may be more vulnerable, these findings across studies suggest that routine screening for attention or concentration problems should be conducted. This could be done during annual comprehensive visits using measures such as the Continuous Performance Test or Trails A and B. Identification of initial deficits or declines in performance over time would signal the need for additional medical tests (MRI) and outreach to schools. If a child with SCD has attentional problems causing difficulties at home and school, medical management of the problem might be considered. This screening must be done in conjunction with an active collaboration with a pediatric neuropsychologist. Future research is needed to document the effectiveness of this approach.

We found no support for our hypothesis that older children with SCD would show greater impairment than younger children. Our findings of no significant age effects are consistent with those of Swift et al. (1989). Wasserman et al. (1991) found a number of age differences but utilized two different tests with disparate item content for the age groups. Both Brown, Buchanan, et al. (1993) and Fowler et al. (1988) reported that older children with SCD performed more poorly than younger children with SCD but only on measures of spatial/constructional functioning and sustained attention. It is feasible that deficits for children with SCD occur early in key neurocognitive domains such as attention/concentration, suggesting the need for early prophylactic transfusion protocols. Unfortunately, all of this work utilized cross-sectional data, so no conclusions can be reached regarding developmental progression (Achenbach, 1978). There is an urgent need for longitudinal investigations of neurocognitive functioning in children with SCD beginning early in the child's life (Wang et al., 1999). Given the modest number of children with SCD followed at individ-
ual hospitals, this work must be completed simultaneou-
ously at multiple collaborating centers and must include 
an appropriate comparison group (Richard & Burlew, 1997).

Findings from this study are limited because the 
data were obtained from one treatment center with 
a small sample of children. Scores for children with 
SCD and for case controls were below the average 
on all standardized tests, so these findings may be 
limited to children with SCD from disadvantaged 
environments. Additional exploratory analyses ex-
amined the relationship between scores on our 
occupation based measure of SES and the level-
of-performance scores. A significant correlation was 
found between the verbal level-of-performance 
score and family social prestige ($r = .32, p < .05$), 
but correlations were not significant for any of our 
other level-of-performance scores. Similar findings 
were obtained using maternal education. These 
findings suggest that family social prestige is not 
playing a key role in the significant findings for at-
tention/memory, but further work is clearly needed.

We also utilized a limited neuropsychological 
battery, so our sensitivity to detect problems was re-
stricted. This was especially the case for our assess-
ment of academic achievement. Future work should 
include a more comprehensive test of academic 
achievement.

These findings are important, given the implica-
tions of impaired cognitive functioning on subse-
quently academic and occupational achievements. 
When the long-term impact of cognitive deficits is 
considered for children with SCD who experience 
chronic fatigue and physical limitations that restrict 
employment opportunities, our findings suggest 
that children with SCD are at risk for future aca-
demic difficulties and occupational restrictions.

In summary, these findings suggest that, com-
pared to case control classmates, children with SCD 
with no overt signs of CNS damage have cognitive 
deficits. Findings from this study suggest that these 
children are at high risk for suboptimal psycho-
social outcomes as adults. A young adult with cog-
nitive deficits and physical limitations may have 
restricted employment possibilities that lead to un-
employment or underemployment. This research 
highlights the cognitive limitations for this group 
of children that may contribute to subsequent dif-
ficulties. The findings from this research and several 
other studies suggest that routine screening of at-
tention and concentration should be completed 
during annual comprehensive care visits. Although 
our data do not provide information regarding the 
age of the child when routine screening should be-

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