Mind matters in pediatric sickle cell disease: evaluation of neurocognitive deficits, behavioral and emotional problems and health-related quality of life
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Neurocognitive deficits in children with sickle cell disease: a comprehensive profile

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Abstract

Aim: Sickle cell disease (SCD) can lead to profound cerebral damage, associated with neurocognitive deficits. The aim of the current study was to evaluate a broad range of neurocognitive functions in children with SCD compared to a SES-matched control group, in order to gain more insight into the specific deficits of these patients.

Methods: Forty-one children with homozygous SCD (HbSS or HbS-β0-thalassemia) and 38 controls were assessed on a comprehensive set of well-defined and validated measures of neurocognitive functioning. Besides general intelligence, we evaluated executive functioning extensively (including response inhibition, sustained attention, planning, visuo-spatial working memory and verbal working memory) as well as visuo-motor functioning.

Results: SCD was clearly associated with lower IQ scores. More than one in three children with SCD had a Full-scale IQ below 75. Furthermore, children with SCD showed deficits in visuo-motor functioning. Some evidence was found for executive dysfunction: Children with SCD displayed poor visuo-spatial working memory, as well as subtle deficits in sustained attention and planning. No significant differences were found between children with SCD and controls in terms of response inhibition and verbal working memory.

Conclusion: Children with SCD are at increased risk of lower intelligence, visuo-motor impairments and executive dysfunction. These neurocognitive deficits may underlie high rates of scholastic impairments in these children. The present findings further illuminate the importance of regular neurocognitive evaluations and future neurocognitive rehabilitation programs for children with SCD.
Introduction

Sickle cell disease (SCD) is a hereditary red blood cell disorder that is characterized by chronic haemolytic anaemia and vascular occlusion, causing pain and irreversible organ damage. The most devastating complication of SCD is cerebral vascular infarction. Although most infarcts are not accompanied by overt neurological symptoms – so-called silent infarcts - they do appear to be associated with diminished neurocognitive functioning (1-3).

Indeed, SCD has been associated with impairments in general cognitive functioning as measured by IQ. Children with SCD and overt strokes seem to be most impaired, with a decrease of approximately 14 Full-scale IQ points (3), while children with silent infarcts have been described to score 4-7 Full-scale IQ points lower than children with normal MRI (4, 5). However, it appears that there are cognitive effects of SCD for children with normal MRI as well (6-8).

In addition to detrimental effects on general cognitive functioning, SCD has been associated with deficits in specific areas of neurocognitive functioning including executive functioning (1, 9-14) and visuo-motor functions (15, 16). Deficits in these two areas are expected, given that silent infarcts commonly occur in frontal lobe white matter, within the border zone between the middle and anterior cerebral artery distribution (17, 18). The frontal lobes play a major role in executive functions, which are higher order cognitive functions including abilities such as response inhibition, planning, working memory, and attention (19). These functions greatly affect other areas of neurocognitive functions and are generally strongly related to academic and behavioral problems. Sustained attention and working memory appear to be particularly vulnerable in children with SCD (1). Response inhibition and planning have been studied less extensively. White matter damage is thought to underlie deficits in visuo-motor functions. Although deficits on this neurocognitive domain have been recognized in children with SCD, findings remain inconsistent (1). Some researchers have reported average motor skills in children with SCD (10, 20) while others found clear deficits compared to healthy controls (15, 16). Many studies investigated either visual-spatial or motor skills, but not both (1).

Although the literature on neurocognitive sequelae of SCD is quite extensive, previous studies have several methodological limitations. Many studies lacked appropriate comparison groups. As the majority of families of children with SCD come from immigrant communities with a low socio-economic status (SES) and are single parented (21), these children are more likely than the general population to grow up in unfavourable circumstances that already place them at higher risk for neurocognitive deficits (3). Although siblings without SCD have been described as the preferable control group for studying the neurocognitive effects of SCD (22), only few researchers incorporated healthy siblings as controls. Furthermore, almost all previous studies on neurocognitive deficits in SCD have been performed in the United States of America. Findings from these studies need to be replicated in Western Europe because of differences in the healthcare and educational system and the origins of the patient population, as SCD...
patients in Western-Europe are mainly new immigrants from Western Africa, while most African-Americans have been living in the US for a long time. Moreover, many studies used restricted assessment batteries: Some studies focused only on general intelligence, whereas others targeted isolated aspects of neurocognitive functioning.

The present study extends previous research by comparing a large group of Dutch children with SCD to a SES-matched control group, comprising healthy siblings of participating children with SCD and healthy siblings of other SCD patients receiving care at our hospital, on a comprehensive set of well-defined and validated measures of key neurocognitive functions.

**Methods**

**Participants**

Forty-one children with SCD and 38 SES-matched controls aged 6 to 18 years participated in the study. A total of 46 children were randomly selected from the children receiving treatment for a severe form of SCD (HbSS or HbS-β0-thalassemia) at the Comprehensive Sickle Cell Care Center of the Emma Children’s Hospital, Academic Medical Center in Amsterdam. From these, 41 patients (89%) participated (5 declined). Most of these had an HbSS genotype (n = 37, 90%), the other four (10%) had an HbS-β0-genotype. Of the children with SCD that were included, three (7%) had previously experienced a symptomatic stroke. Six children (14%) received scheduled blood transfusion, either for stroke (n = 4) or intracranial arterial stenoses detected on MRI (n = 2). The clinical condition of all children with SCD was stable at the time the neurocognitive assessment took place.

After recruitment of participants with SCD, SES-matched controls were recruited. Fifty-seven healthy children were invited to participate. From these, 38 (67%) participated. First, we recruited healthy (full or half-) siblings of the group of participating children with SCD. These siblings were matched for age and gender one by one to participants. As no sibling match was available for all participating children with SCD, we recruited 19 additional controls (50%), who were healthy siblings from non-participating children with SCD receiving care at our hospital. These controls had similar demographic characteristics and were matched for age and gender one by one to participants as well. Inclusion took place between October 2007 and October 2008.

**Procedure**

The medical ethics committee of the Academic Medical Center in Amsterdam approved the study protocol. Written informed consent was obtained from parents and children aged twelve years and older. Administration of the neurocognitive tests was performed in a fixed order by trained examiners using standardized instructions. Administration of the entire test battery (including breaks) required a maximum of three and an half hours.
Neurocognitive measures

Intelligence

Full-scale IQ was estimated by four subtests of the Wechsler Intelligence Scale for Children-III (23) or the Wechsler Adult Intelligence Scale-III (24) (depending on the child’s age): Vocabulary, Arithmetic, Block Design and Picture Arrangement. These subtests correlate in the low to mid .90’s with Full-scale IQ and therefore give a reliable estimate of Full-scale IQ. Verbal IQ was estimated by Vocabulary and Arithmetic, and Performance IQ was estimated by Block Design and Picture Arrangement.

Executive Functioning

Response inhibition and sustained attention

Response inhibition and sustained attention were measured using the Stop task (25, 26). This task requires the child to react as quickly and accurately to airplanes appearing on a computer screen and to occasionally inhibit a response upon presentation of a visual stop signal. Response inhibition was measured by stop signal reaction time (SSRT, an estimate of the speed of the inhibitory response). Sustained attention was measured by the number of errors, and by mean reaction time (MRT) of correct responses, which was calculated for the first, second, third, and fourth part of the task.

Planning

Planning ability was investigated using an adapted version of the Tower of London (ToL; (27)), with multiple difficulty levels. This task requires the child to rearrange three coloured balls on three vertical pegs of different lengths, to transform an initial configuration of the balls into a ‘tower’, in which the balls are arranged on a designated peg. The child has to plan the sequence of moves, as there are constraints on the number of moves and trials allowed to solve the problem. The main outcome measure was the ToL score, which is based on the number of trials required to solve a problem. Additional outcome variables were Planning time (the time between presentation of an item and initiation of the first move) and Execution time (the time between initiation of the first move and completion of the final move). It was expected that Planning and Execution time would increase with higher difficulty levels.

Working memory

Visuo-spatial working memory was measured with a spatial variant of the computerized N-back task (28-30). Children were presented with a picture of an apple with four holes in it, from which a caterpillar appeared. Children were instructed to press one of four response buttons corresponding to the hole in which they had seen the caterpillar one move back (1-back condition) up to four moves back (4-back condition). A maximum of four blocks (of 32 trials each) was administered, preceded by a practice block of 10 trials. Total number of correct responses was used as measure of visuo-spatial working memory.
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Verbal working memory was measured with the maximum span on Digit span forwards and backwards of the WISC-III (23) or WAIS-III (24) (depending on the child’s age). The forward part was administered first and consisted of repeating sequences of numbers increasing in length in the exact same order. For the backward part, children had to repeat sequences of numbers increasing in length in the reverse order.

Visuo-motor functioning
Visuo-motor functioning was assessed using the Beery-Buktenica Developmental Test of Visual-Motor Integration (Beery VMI; (31)). In the Beery VMI children have to reproduce 30 geometric shapes with graded difficulty as accurately as possible. Total score was used as outcome measure.

Data Analysis
The Statistical Package for the Social Sciences (SPSS version 16.0) was used to manage and analyze the data. All neurocognitive outcome measures were normalized by applying a Van der Waerden transformation. An independent t-test and Chi square tests were used to compare children with SCD to controls on demographic characteristics.

Linear mixed models were used to analyze differences between children with SCD and controls on the measures derived from the neurocognitive tasks. The linear mixed model allows for the investigation of group differences while controlling for the non-independency of data (i.e. more than one child participated per family, which resulted in related measurements within groups and between groups). All neurocognitive measures (except for IQ scores) were analyzed using group and age as fixed factors and family as random effect to account for within family correlation. Age was included in the model because of the broad age range of the subjects in the study and age-corrected standardized scores were not available for all neurocognitive measures. For IQ scores, only group was included as fixed factor, as analyses were performed with age-corrected standardized scores. Since Planning and Execution time on the ToL were obtained for multiple difficulty levels, difficulty level was added to the model as additional fixed factor. The group by difficulty level interaction was studied to determine group differences in the effects of increasing difficulty levels on task performance. A second random effect (random intercept per patient) was added, to account for the correlation between measurements belonging to the same patient. Similarly, to analyse group differences in sustained attention, MRTs derived form the first through fourth part of the Stop task were analysed with task part as additional fixed factor and an additional random intercept per patient. P values < 0.05 were considered significant. Effect sizes (d) were calculated by dividing the difference in mean score between children with SCD and controls by the pooled standard deviation of both groups. According to Cohen (32), effect sizes < 0.2 are considered small, effect sizes > 0.5 and < 0.8 moderate, and effect sizes > 0.8 large.
Results

Demographics

Table 1 provides the demographic characteristics of children with SCD and controls. The groups did not significantly differ in age, gender, country of origin, parental marital status, maternal educational level or parental paid employment.

Neurocognitive domains

Table 2 describes the results for the two groups on the neurocognitive measures.

Intelligence

Children with SCD had a lower mean Full-scale IQ than controls. They also had a lower mean Performance IQ and Verbal IQ. The mean Full-scale IQ of controls was just below the average range compared to population norms, whereas the mean Full-scale IQ of children with SCD was more than 1.5 SD below the population average. The distribution of Full-scale IQ scores of children with SCD and controls is presented in Figure 1.

Table 1. Demographic characteristics of children with SCD and SES-matched controls

<table>
<thead>
<tr>
<th></th>
<th>Children with SCD (n = 41)</th>
<th>SES-matched controls (n = 38)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years, M (SD)</td>
<td>12.2 (3.1)</td>
<td>11.6 (3.3)</td>
</tr>
<tr>
<td>Boys, n (%)</td>
<td>21 (51)</td>
<td>19 (50)</td>
</tr>
<tr>
<td>Country of origin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surinam, n (%)</td>
<td>18 (44)</td>
<td>24 (64)</td>
</tr>
<tr>
<td>West/Central Africa, n (%)</td>
<td>20 (49)</td>
<td>10 (26)</td>
</tr>
<tr>
<td>Turkey, n (%)</td>
<td>2 (5)</td>
<td>2 (5)</td>
</tr>
<tr>
<td>Netherlands Antilles, n (%)</td>
<td>1 (2)</td>
<td>2 (3)</td>
</tr>
<tr>
<td>Parental marital status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married/living together, n (%)</td>
<td>15 (37)</td>
<td>18 (47)</td>
</tr>
<tr>
<td>Single, n (%)</td>
<td>26 (63)</td>
<td>20 (53)</td>
</tr>
<tr>
<td>Highest level of education of mother a</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lower, n (%)</td>
<td>23 (56)</td>
<td>20 (53)</td>
</tr>
<tr>
<td>Intermediate, n (%)</td>
<td>6 (15)</td>
<td>11 (29)</td>
</tr>
<tr>
<td>Higher, n (%)</td>
<td>2 (5)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Not specified, n (%)</td>
<td>10 (24)</td>
<td>6 (16)</td>
</tr>
<tr>
<td>Parental paid employment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes, n (%)</td>
<td>22 (54)</td>
<td>24 (63)</td>
</tr>
<tr>
<td>No, n (%)</td>
<td>17 (42)</td>
<td>10 (26)</td>
</tr>
<tr>
<td>Not specified, n (%)</td>
<td>2 (5)</td>
<td>4 (11)</td>
</tr>
</tbody>
</table>

Group differences were tested for: age, gender, country of origin, parental marital status, highest level of education of mother, and parental paid employment. None of the group comparisons were significant, all effect sizes were small. a Education: Lower = elementary education, general secondary education junior-level, lower vocational education; Intermediate = general secondary education-senior level, and vocational education-junior level; Higher = vocational education-senior level and university education.
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Table 2. Performance on neurocognitive measures of children with SCD and SES-matched controls

<table>
<thead>
<tr>
<th>Neurocognitive Measure</th>
<th>Children with SCD (n = 41)</th>
<th>SES-matched controls (n = 38)</th>
<th>Group differences</th>
</tr>
</thead>
<tbody>
<tr>
<td>IQ</td>
<td>M  SD</td>
<td>M  SD</td>
<td>d     df       p</td>
</tr>
<tr>
<td>Full-scale IQ</td>
<td>80 12.5</td>
<td>88 13.1</td>
<td>0.6   47.85     &lt;0.001</td>
</tr>
<tr>
<td>Verbal IQ</td>
<td>83 12.1</td>
<td>93 15.1</td>
<td>0.7   46.84     &lt;0.001</td>
</tr>
<tr>
<td>Performance IQ</td>
<td>79 14.6</td>
<td>86 10.6</td>
<td>0.6   54.87     0.010</td>
</tr>
<tr>
<td>Response inhibition</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stop signal reaction time</td>
<td>225 59.2</td>
<td>222 50.18</td>
<td>0.1   71.00     0.408</td>
</tr>
<tr>
<td>Errors on Stop task</td>
<td>4 5.6</td>
<td>3 4.3</td>
<td>0.2   3.90      0.053</td>
</tr>
<tr>
<td>MRT on Stop task (averaged across experimental blocks)</td>
<td>552 117.3</td>
<td>550 107.1</td>
<td>&lt;0.1  70.32     0.968</td>
</tr>
<tr>
<td>Planning</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ToL score</td>
<td>46 9.9</td>
<td>47 9.3</td>
<td>0.1   48.07     0.012</td>
</tr>
<tr>
<td>Planning time on ToL (averaged across difficulty level)</td>
<td>22 19.5</td>
<td>28 32.9</td>
<td>0.2   199.86    0.404</td>
</tr>
<tr>
<td>Execution time on ToL (averaged across difficulty level)</td>
<td>54 21.7</td>
<td>52 21.7</td>
<td>0.1   235.06    0.002</td>
</tr>
<tr>
<td>Visuo-spatial working memory</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N-Back task correct responses</td>
<td>48 25.9</td>
<td>57 28.3</td>
<td>0.3   65.14     0.005</td>
</tr>
<tr>
<td>Verbal working memory</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Digit span forwards</td>
<td>8 1.6</td>
<td>8 1.5</td>
<td>&lt;0.1  68.08     0.099</td>
</tr>
<tr>
<td>Digit span backwards</td>
<td>5 1.9</td>
<td>5 1.8</td>
<td>&lt;0.1  60.93     0.552</td>
</tr>
<tr>
<td>Motor functioning</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beery VMI total score</td>
<td>22 3.9</td>
<td>23 4.1</td>
<td>0.3   55.30     0.015</td>
</tr>
</tbody>
</table>

Note. Effect sizes (d) were calculated by dividing the difference in mean score between children with SCD and SES-matched controls by the pooled standard deviation of both groups. SCD = Sickle Cell Disease, MRT = Mean Reaction Time, ToL = Tower of London, VMI = Visual-Motor Integration. P-values derived from linear mixed models.

Exploratory analyses showed that more than one in three children with SCD (32%) had a Full-scale IQ below 75, versus one in ten controls (10%) ($\chi^2 (1) = 5.239, p = 0.022$).

Executive Functioning

Response inhibition and sustained attention

No group differences were found in SSRT on the Stop task, indicating no differences between children with SCD and controls in response inhibition. Groups did not differ in MRT across the four parts of the task and there was no evidence of a greater decline in MRT across the four parts of the task in the SCD group compared to the control group. The difference between children with SCD and controls on Errors almost reached significance, indicating somewhat lower levels of sustained attention in children with
SCD. Age was associated with task performance ($p < 0.001$), with older children performing better than younger children on all measures of the Stop task.

**Planning**
Children with SCD obtained a slightly but significantly lower ToL score than controls, indicating somewhat poorer planning ability. Compared to controls, children with SCD used 6 seconds less Planning time and 2 seconds more Execution time on average to solve an item. Only the difference in Execution time reached statistical significance. Moreover, the increase in difficulty level had a differential effect on the Execution time of both groups. With increasing difficulty levels, children with SCD took less time to execute an item, while controls effectively took more time ($p = 0.037$). Age contributed significantly to both the ToL score and Execution time, with older children performing better ($p < 0.001$). Age did not significantly contribute to Planning time ($p = 0.902$).

**Working memory**
Results from the N-Back task revealed that children with SCD made less correct responses than controls, indicating poorer visuo-spatial working memory. However, no group differences were found in verbal working memory. Children with SCD and controls achieved a similar score on both Digit span forwards and backwards. Age was associated with performance on both working memory tasks ($p < 0.001$ on N-Back task, $p = 0.004$ on Digit span forwards, and $p = 0.003$ on Digit span backwards), with older children performing better.

**Visuo-motor functioning**
Children with SCD obtained a lower total score on the Beery VMI compared to controls, indicating deficits in visuo-motor functioning. Older age was associated with better performance ($p < 0.001$).
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Discussion

This study provides evidence that children with SCD perform worse than SES-matched controls on several well-defined and validated measures of key neurocognitive functions. SCD is clearly associated with lower intelligence and deficits in visuo-motor functioning compared to controls. Some evidence was found for executive dysfunction: Children with SCD displayed poor visuo-spatial working memory, as well as subtle deficits in sustained attention and planning. No significant differences were found between children with SCD and controls in terms of response inhibition and verbal working memory.

Our study adds to the existing literature with the finding that children with SCD had lower Full-scale, Verbal and Performance IQ's compared to SES-matched controls. In a meta-analysis of 10 studies using sibling controls, the mean Full-scale IQ of children with SCD was established at 87 (SD 14), compared to a mean Full-scale IQ of 91 (SD 13) for healthy siblings (6), which is a surprisingly small difference. Although the mean Full-scale IQ of our control group, for 50% comprised of healthy siblings, is comparable to these results (88, SD 13), we found a lower mean Full-scale IQ for children with SCD (80, SD 13).

This contrast could be explained by the age of our study sample. In our study, children with SCD were approximately one to three years older than the children in most of the studies in the meta-analysis. Previous results showed lower IQ's in older samples (11-13 years) than in younger samples (9-10 years and 10-11 years), suggesting a decline in cognitive functioning with increasing age (6). Survivors of childhood cancer have similarly been described to show a decline in cognitive functioning with increasing age and developmental stage (33). Future longitudinal studies should provide more insight in this issue. Another explanation for the lower mean Full-scale IQ in our study sample could be that, in the present study, there might have been more children with silent infarcts than in the studies reviewed by Schatz et al. (6). This possibility can not be ruled out since the present study, as well as a number of studies reviewed by Schatz et al., did not establish the presence of silent infarctions using MRI. These children may represent a subgroup with a lower Full-scale IQ.

It is particularly striking that one in three children with SCD had a Full-scale IQ below 75, which clinically would be described as having a learning disability. This percentage is similar to the percentage reported in a French study (5) and is expected to have profound consequences for academic functioning. It is surprising to note, however, that relatively few children with SCD in our sample (14%) received special educational services.

In contrast to our expectations, mixed evidence was found for deficiencies in executive functioning. Most researchers investigating executive functions of children with SCD focused on mental flexibility and sustained attention, overlooking other relevant frontal lobe functions such as response inhibition and planning (9-12, 34). The results of the present study failed to find support for deficits in response inhibition and verbal working memory. Previously, infarcts associated with SCD resulted in impaired memory span in some but not all children; the pattern of performance varied depending on lesion location (35). Verbal working memory of children with anterior or posterior lesions was
comparable to children without infarcts, while children with infarcts in diffuse regions of
the brain performed less well. We did observe that children with SCD displayed difficulties
in visuo-spatial working memory, and subtle deficits in sustained attention and planning
compared to SES-matched controls. As the general relationship between executive
functioning deficits and externalizing behaviour disorders has been firmly established
(36), these subtle deficits in executive functioning might be related to results of our
previous work, showing that some children with SCD display externalizing behaviour
problems, particularly at school (37). However, effect sizes of executive function deficits
were small. It will be relevant to distinguish children with and without infarcts and to
differentiate according to lesion location in future studies, especially when investigating
this neurocognitive domain.

Children with SCD showed deficits in visuo-spatial working memory and visuo-motor
functioning compared to SES-matched controls. These deficits have previously been
observed in children with SCD (14, 16, 34), although findings in this area have been
remarkably inconsistent (3, 12, 38). In the present study, a visual working memory
measure was chosen that is relatively independent of motor-functioning (N-Back task)
and an instrument to assess visuo-motor functioning was included as well (Beery VMI), as
was recently recommended (16). Interestingly, deficits appeared on both tasks, leading
us to speculate that children with SCD might have a specific deficit in the perception of
visuo-spatial information. No deficits were found on verbal working memory. Visuo-motor
cognitive abilities generally appear to be more affected than auditory-verbal abilities in
children with SCD (1, 3), which is confirmed by the results of the present study.

While interpreting the results of this study, limitations and strengths should be taken
into account. A first limitation was that the recruitment of age- and gender matched
healthy siblings from participating children with SCD appeared less feasible than we
expected. This caused us to recruit healthy siblings in families from non-participating
children with SCD as controls, who were comparable in terms of SES as they were
coming from the same neighborhood. Consequently, in our control group, children
from Surinam descent seemed somewhat overrepresented compared to the SCD group.
Nevertheless, the groups did not significantly differ in country of origin, and IQ scores of
controls were comparable to those found in other comparison groups of healthy siblings.
Moreover, within-group analyses in both patients and controls revealed no significant
differences with small effect sizes between children from Surinam or African descent on
any of the neurocognitive measures. Suggestions to strengthen future research designs
would be to perform multicenter studies, to expand the participant pool and thereby
increase feasibility regarding the inclusion of age- and gender matched healthy siblings
from participating children with SCD. Additionally, longitudinal designs would allow the
consideration of developmental aspects of neurocognitive functioning in children with
SCD. Another limitation was the lack of MRI data. Correlating biological parameters, like
MRI data and severity of the anaemia to neurocognitive outcome measures will be a
future direction of our work, which will hopefully provide more insight into the causes of
the neurocognitive deficits observed.
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Strengths of this study were that we assessed a broad range of neurocognitive functions, using well-defined and validated measures, providing a comprehensive neurocognitive profile of children with SCD. As healthy siblings have been described as the preferable control group, we included a control group comprising healthy siblings of participating children with SCD and healthy siblings of other SCD patients receiving care at our hospital. Moreover, we used robust statistical methods that took within family correlations into account.

Our findings demonstrate evidence that SCD is associated with significant deficits in general cognitive functioning, as well as subtle deficits in executive functioning. Furthermore, our findings suggest that visuo-motor abilities might also be prone to impairments in SCD. The results of this study stress the importance of implementing routine neurocognitive evaluation in daily clinical practice. This, together with brain imaging evaluations, would result in earlier detection of those children at higher risk for neurocognitive problems, preferably followed by close monitoring and early intervention (39). Until now, few interventions have been developed (see (40), for a review). Neurocognitive rehabilitation could help children with SCD to compensate for their limitations, which could contribute significantly to the quality of life of these children.

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References


