Effects of Diabetes on Learning in Children

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ABSTRACT. *Objective.* **Subtle neuropsychological deficits have been found in some children with type 1 diabetes. However, these data have been inconsistent, and it is not clear what the impact of these deficits might be on the learning of children with diabetes over time. The purpose of this study was to determine whether type 1 diabetes significantly interferes with the development of functional academic skills. It was hypothesized that 1) children with type 1 diabetes would demonstrate deficits in academic performance and behavior when compared with sibling or classmate control subjects and 2) that academic performance in children with type 1 diabetes would decline slightly but significantly over time whereas the performance of siblings or classmates would not.**

Methods. **Three groups of children from 5 pediatric diabetes clinics in a primarily rural Midwestern state participated in this study: children with type 1 diabetes (n = 244), a sibling control group (n = 110), and an anonymous matched classmate control group (n = 209). The mean age of the children with diabetes was 14.8 years (standard deviation: 3.2) and of the siblings was 14.6 years (3.2); the mean grades were 8.1 (2.9) for the children with diabetes and 7.9 (3.1) for the siblings. The Hollingshead 2-factor index revealed that the children were from primarily middle- to upper-middle-class families. The mean age of onset of diabetes for the children with diabetes was 8.3 years (3.7) with a mean disease duration of 7.1 years (3.9). Because the matched classmate data were obtained anonymously, demographic information was not available on this group. Academic achievement was measured using both standardized tests and data on classroom performance. The standardized test data included scores from the Iowa Tests of Basic Skills (ITBS) for grades 3 through 8 and the Iowa Tests of Educational Development (ITED) for grades 9 through 12. Scores in 3 broad academic areas that are obtained on children of all ages were examined: math, reading, and core total (a composite score of reading, language, and math). ITBS/ITED data were obtained on all participants. School data including the number of days absent, school years repeated, and grade point averages for math and reading were obtained on the children with diabetes and their siblings. A short, 50-item screening scale (PBS-50d), adapted from the longer 165 item Pediatric Behavior Scale (PBS), was completed by the parents to obtain information on the behavioral characteristics of the children with diabetes and their siblings. Diabetes variables measured included metabolic control (HbA1c), age at onset, and disease duration. This study looked at both the current academic performance of children with diabetes and their performance over time in relation to 2 control groups: siblings and matched classmates. A cross-sectional approach was used to evaluate current performance. Statistical differences between groups were evaluated using matched t tests or McNemar's test for differences between related samples as appropriate. Differences across time were evaluated using hierarchical linear modeling. Comparisons of ITBS/ITED test scores across grades used national percentile ranks that were converted to standard scores (SS) with a mean of 100 and a standard deviation of 15. Students in this study performed above the national average, which is typical of students in the state where this study was conducted. Data from participating clinics were compared, and no differences in current achievement scores, grade point averages, or socioeconomic status were noted for either children with diabetes or their siblings. Therefore, all subsequent analyses used data combined from all sites.**

Results. **Current academic performance on the ITBS/ITED did not show lower performance by children with diabetes compared with either control group; in fact, children with diabetes performed better than their siblings on math (mean SS: 115.0 vs 111.1) and core total scores (mean SS: 113.9 vs 110.5) and better than their matched classmates on reading (mean SS: 108.9 vs 106.8). When subgroup comparisons based on diabetes metabolic control were made among children with diabetes, poorer academic performance tended to occur in children with poorer diabetic control. However, this pattern was also noted in sibling scores when the siblings were grouped on the basis of the level of diabetic control of their brother or sister with diabetes. Children with diabetes had significantly more school absences (Mean = 7.3 per year) than their siblings (M = 5.3) and more behavioral problems. Behaviorally, the 2 groups did not differ on the 4 general factors of Aggression/Opposition, Hyperactivity/Inattention, Depression/Anxiety, and Physical Complaints. However, children with diabetes did differ significantly from their siblings on items that reflected compliance, mood variability, and fatigue, but not learning. These were 4 areas included in the PBS-50d to reflect potential concerns for children with diabetes. Academic achievement growth curves for the ITBS/ITED for each group revealed no statistically significant differences between groups when tested using hierarchical linear modeling. Individual differences in the growth trajectories were too small and inconsistent to be detected.**

Conclusions. **For most children, type 1 diabetes is not associated with lower academic performance compared with either siblings or classmates, although increased behavioral concerns are reported by parents. The results**

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of this study suggest that the subtle cognitive deficits often documented in children with type 1 diabetes may not significantly limit the functional academic abilities of these children over time. However, careful monitoring is still needed to ensure that episodes of hypoglycemia associated with seizures are not adversely affecting learning. ***Pediatrics*** **2002;109(1). URL: http://www.pediatrics.org/cgi/content/full/109/1/e9;** ***type 1 diabetes, academic achievement, children.***

ABBREVIATIONS. SES, socioeconomic status; ITBS, Iowa Tests of Basic Skills; ITED, Iowa Tests of Educational Development; GPA, grade point average; HbA1c, glycosylated hemoglobin; HLM, hierarchical linear modeling; PR, percentile rank.

Type 1 diabetes occurs in approximately 1 in 800 children,[1] and there is evidence that the incidence of type 1 diabetes is increasing worldwide.[2] Children with type 1 diabetes must deal with a complicated routine of daily insulin injections along with monitoring blood glucose levels, dietary intake, and exercise. All of this must be conducted while the child still lives a "normal" life. Chronic, extreme fluctuations in blood sugar levels and the psychosocial effects of a chronic disease have been associated with deficits in academic performance. For children with diabetes, life will not be normal if their learning and school performance are compromised by cognitive deficits resulting from their disease. Therefore, it is crucial that the impact of diabetes on learning in children be determined.

Early studies of the cognitive abilities of children with type 1 diabetes focused on the children's general intellectual abilities. Although the results of these early studies were somewhat contradictory, probably as a result of sampling biases,[3,4] subsequent studies reported that children with diabetes typically perform in the normal range on standardized intelligence tests.[5] In a recent study by Northam et al,[6] overall IQ of children with diabetes at the time of diagnosis was the same as a control group of well children matched on socioeconomic status (SES) and age. At 2 years postdiagnosis, children with diabetes, particularly children with early disease onset, showed less positive changes than the control group. It is now generally thought that as a group, children with diabetes function within the same range of intelligence as the general population, but more subtle cognitive deficits may be present.[5,7–10] Also, children with the onset of diabetes early in life, before 5 to 7 years of age, have been found in some cases to perform lower on overall intelligence.[3,7,10]

A number of studies have reported differences between groups of children with diabetes and other groups on specific neuropsychological tests. Difficulties have been reported with verbal intelligence,[9] slow work rate,[9] memory skills,[5,7] timed motor tasks,[10] visuospatial abilities,[6,10–12] abstract/visual reasoning,[13] speed of processing,[6] and attention.[5,14] However, these results have been contradictory; some studies have identified verbal and memory difficulties, whereas others have failed to find verbal difficulties and have instead identified visuospatial deficits. Neuropsychological deficits have been associated with a number of risk factors, most commonly onset of type 1 diabetes before the age of 7[5,7,10,11,15] and psychosocial factors such as increased school absences.[12,16] Ryan[17] noted that children with early-onset diabetes tend to have spatial difficulties, whereas children with later onset have difficulties with verbal abilities, school achievement, and psychomotor skills. These differences in neuropsychological symptoms may be related to age and associated risk factors, such as hypoglycemic episodes in children with early disease onset and hyperglycemia and social burden for children with later onset of diabetes.

The impact of these contradictory neuropsychological findings on the overall academic functioning of children with diabetes has resulted in inconsistent conclusions. An early study that examined academic achievement, as well as intelligence, in children with type 1 diabetes and their siblings[18] reported that the 2 groups were similar in both areas. More recent studies have questioned that finding, suggesting that children with diabetes are at risk for academic difficulties. Children with diabetes have been found to score lower on a national achievement test than several small comparison groups of children with other chronic diseases.[19] Reading difficulties have been noted in children with diabetes,[20] with more reading problems occurring in children who were younger at the time of disease onset compared with children who had later onset of the disease.[7,10,21] Whereas these studies evaluated word recognition or teacher report of reading, Hagen et al[5] found that children with late-onset diabetes performed significantly below the age-matched, nondiabetic children in their control group on reading comprehension. In studies of academic achievement that have assessed arithmetic abilities, there have been mixed results, with some finding no significant difficulties in arithmetic[5,10] and others reporting slightly but significantly lower arithmetic abilities in children with diabetes compared with control children.[12] Gender differences have been noted within groups of children with diabetes, with some reporting boys with diabetes performing significantly lower on measures of attention and learning than girls with diabetes,[21] whereas other studies have found no gender differences.[10]

Kovacs et al,[22,23] in a longitudinal study of cognitive and academic abilities in children with type 1 diabetes, reported that at the time of diagnosis, the children performed within the average range in cognitive abilities and school grades but that over time, vocabulary and grades tended to decline while nonverbal performance tended to improve. It is interesting that a control group of children who were referred for psychological evaluation showed similar patterns of change in their verbal and nonverbal skills but not in their school grades. Kovacs et al hypothesized that these findings resulted from deficits in short-term memory associated with episodes of moderate hypoglycemia not reflected in HbA1c levels[23] or from the "psychosocial burden" of type 1 diabetes.[22] Other researchers have noted psychosocial concerns in children with diabetes. Holmes et al[24] reported that children with diabetes have slightly higher scores than children without diabetes matched on grade, race, and gender on a behavior rating scale, although both groups were in the normal range and the between-group differences were no more than 2 to 3 T-score points, approximately ¼ standard deviation. Grey et al[25] found that children with diabetes were depressed, dependent, and withdrawn at the time of diagnosis; were within the normal range 1 year postdiagnosis; but again showed some depressive symptoms 2 years after diagnosis. Northam et al[26] also reported that children with diabetes were mildly distressed at the time of diagnosis but that this had resolved by 1 year postdiagnosis.

In summary, there is substantive evidence to suggest that although children with type 1 diabetes perform in the average range as a group on tests of general intelligence, they may show mild cognitive and academic difficulties, particularly in reading. Although subtle neuropsychological deficits have been found in some children with type 1 diabetes, these data have been inconsistent, and it is not yet clear what the impact of these deficits might be on the learning of children with diabetes over time. Unfortunately, previous studies of learning deficits in children with diabetes have often used small, selective clinical samples, cross-sectional designs, and incompletely matched control groups, which have contributed to the markedly inconsistent results.

The purpose of this study was to determine whether type 1 diabetes significantly interferes with the development of functional academic skills. A large, representative sample of children with type 1 diabetes was compared with 2 control groups: siblings and classmates. The specific hypotheses tested were 1) that children with type 1 diabetes demonstrate deficits in academic performance and behavior when compared with sibling or classmate control subjects and 2) that academic performance in children with type 1 diabetes declines slightly but significantly over time when compared with sibling or classmate control subjects, as the physiologic effects and psychological burden of this chronic disease influence long-term achievement.

METHODS

Setting and Study Groups

Five pediatric/pediatric endocrinology/diabetes clinics in a primarily rural Midwestern state participated in this study. Three groups of children were studied: children with type 1 diabetes (n = 244), a control group of siblings of the children with diabetes (n = 110), and a control group of classmates matched with the children with diabetes (n = 209).

Children With Type 1 Diabetes

Children in the type 1 diabetes group had diabetes for at least 1 year, were typically treated with conventional therapy of 2 shots per day, were ages 8 to 18 years at the time of the first data point, had taken the Iowa Tests of Basic Skills (ITBS) and the Iowa Tests of Educational Development (ITED) in the past 2 years, and had no other chronic health conditions.

Sibling Control Group

For each child with diabetes, efforts were made to identify a sibling without diabetes, within 4 years of age of the child with diabetes, who had also taken the ITBS/ITED. As expected, not all of the 244 children with diabetes had siblings who fit the inclusion criteria. The use of sibling control subjects allowed for some control of genetic factors and home environment.

Matched Classmate Control Group

Where possible, an anonymous matched classmate was identified for each child with diabetes using data from the first year that the child with diabetes took the ITBS. Classmates were matched on gender, age, and similarity in ITBS scores at that time as well as being from the same grade and school as the child with diabetes. Of the children who had a matched classmate, 78% were matched in grade 3 and all but 5 of the remaining children were matched in grades 4 through 6. At the time of matching, 60% of the children with diabetes had already been diagnosed with diabetes. There were no significant differences in achievement between the 60% of children whose diabetes was diagnosed before matching and the 40% whose diabetes was diagnosed after matching. Reasons for not being able to identify a matched classmate for a child with diabetes included children from a neighboring state who took tests other than the ITBS/ITED and children who did not take any standardized tests. The only data available on the matched classmates group were standardized achievement data from the ITBS or ITED. The use of classmate control subjects allowed for control of school curriculum and community environment.

The total group of children with diabetes (n = 244), the children with diabetes who had no siblings in the study (n = 134), the children with diabetes with a sibling (n = 110), and the sibling control group (n = 110) were compared on age, current grade, and SES (see Table 1). These groups were similar in all areas. Both the children with diabetes group and the sibling group were 53% boys and 47% girls. The mean ages of the subgroups ranged from 14.6 (standard deviation: 3.2) to 14.9 (3.5) years, and the mean grades were 7.9 (3.1) to 8.1 (2.9). The Hollingshead 2-factor index revealed that all groups were from primarily middle- to upper-middle-class families.[27] The mean age of onset of diabetes for the total group of children with type 1 diabetes was 8.3 years (3.7) with a mean disease duration of 7.1 years (3.9). Because the matched classmate data were obtained anonymously, demographic information was not available on this group.

Measures

Data were obtained on academic performance, behavioral adjustment, and, for the children with diabetes, disease-related vari-

TABLE 1. Descriptive Information

	All Children With Diabetes (n = 244)		Children With Diabetes Without Sibling (n = 134)		Children With Diabetes With a Sibling (n = 110)		Siblings (n = 110)	
	Mean	Standard Deviation	Mean	Standard Deviation	Mean	Standard Deviation	Mean	Standard Deviation
Age	14.8	3.2	14.9	3.5	14.7	2.7	14.6	3.2
Grade	8.1	2.9	8.2	3.1	8.0	2.6	7.9	3.1
SES*	2.6	0.9	2.6	0.9	2.5	0.8	2.5	0.8
Onset age	8.3	3.7	8.4	4.0	8.3	3.4	NA	NA
Duration	7.1	3.9	7.1	4.0	7.1	3.8	NA	NA

* Hollingshead 2 Factor Index. NA indicates not applicable.

ables. Data on school performance and diabetes variables were obtained from school and medical records. This information was supplemented with a brief demographic questionnaire and a standardized instrument for assessing behavioral concerns in children with chronic health conditions.

Demographic Questionnaire

The demographic questionnaire was completed by a parent to provide basic information about the child with diabetes and any sibling control subjects. This included information on academic and medical history as well as SES. Academic information included a history of grade retention, educational testing, and use of special educational services. Medical history included age at onset of diabetes and number of hospitalizations. Social history included parents' education and occupation. Obtaining information from both the child's record and the parental history provided verification of information.

Academic Achievement

The primary measures of academic achievement were the objective, standardized achievement test batteries, the ITBS,[28] designed for children in grades K to 8, and the ITED,[29] administered to high school students. The ITBS/ITED are test batteries that consist of up to 13 tests in several subject areas that have been standardized with the same normative group of students at each grade. All questions are multiple-choice with 4 or 5 response options. These tests take up to 6 hours to complete and are administered in schools to classes of students over several days. They provide objective, norm-referenced information about the development of the skills that are the foundation of learning. Norms allow student achievement levels to be compared with a nationally representative student group.[30] These batteries are nationally recognized as valid and reliable measures of academic achievement.

For the purposes of this study, not all ITBS/ITED test results were used. The tests that were used were chosen because they allowed comparison of children across a wide age range. The scores in 3 broad academic subject areas that are obtained on children of all ages were examined: math, reading, and core total (a composite score of reading, language, and math). For the tests being used in this study, coefficient alphas range from 0.80 to 0.98.[30]

Parents were asked to provide permission to obtain school records on the children with diabetes and their siblings. These records provided access to ITBS/ITED scores, along with number of days absent, grade point averages (GPAs) from report cards, grades repeated, previous educational testing, individualized educational programs, and use of special services such as the resource room. Grades from report cards were converted to a common scale ranging from 0 to 4, with 0 equal to very poor, or F, grades and 4 equal to excellent, or A, grades.

Behavioral/Emotional Adjustment

The behavioral and emotional adjustment of the children with diabetes and their siblings was assessed through a standardized behavior rating scale. A short, 50-item screening scale (PBS-50d), adapted from the complete Pediatric Behavior Scale (PBS),[31] was used to obtain information on the behavioral characteristics of the children with diabetes and their siblings. The PBS, consisting of 165 items, is a rating scale completed by parents and developed specifically to evaluate behavior problems in children with health problems. Each item is scored on a 0- to 3-point scale, with 0 indicating no problems and 3 indicating that a behavior is very often or very much a problem. The PBS-50d includes 30 items that cover 4 major areas of behavioral/emotional adjustment: Aggression/Opposition, Hyperactivity/Inattention, Depression/Anxiety, and Physical Complaints. Internal consistency coefficients for the four general factors are 0.83, 0.87, 0.80, and 0.73, respectively. Twenty additional items from the complete PBS that assess problems common in children with diabetes were added to the 30 general items. These additional items assessed 4 areas: mood variability, fatigue, compliance, and learning.

Diabetes Variables

For children with diabetes, age at onset of diabetes and diabetic control as measured by glycosylated hemoglobin (HbA1c) were obtained from medical records and the parent questionnaire. HbA1c reflects the average blood glucose level over the preceding 2 to 3 months. In the nondiabetes population, the typical HbA1c level is between 4.5% and 6.0%. In children with diabetes, lower percentages, those close to the nondiabetic range, indicate good metabolic control. Poorer metabolic control is reflected in higher percentages of HbA1c.[32] HbA1c levels are typically obtained on children during routine clinic visits, every 3 to 4 months. All HbA1c's recorded in the medical record were noted, and a mean HbA1c was calculated for each academic year for each child.

In summary, ITBS/ITED data were obtained on the children with diabetes and their siblings and matched classmates. School data, including days absent, grades repeated, GPAs, special educational programming, and behavioral data, were obtained on the children with diabetes and their siblings. Diabetes data, HbA1c and age at onset, were obtained on the children with diabetes.

Procedures

After approval from the Institutional Review Board was obtained, the following procedures were followed. Procedures used in this study required a minimal amount of time from the families to maximize the number of children included in the study.

Primary Site

At the primary site, a designated clinic doctor or nurse asked families during a routine visit whether they would be interested in participating in this study. When a family was interested, the research nurse provided the family with information on the study and obtained written consent from a parent and assent from the child. Parents were asked to complete, for both the child with diabetes and a sibling, the brief Parent Questionnaire, a PBS-50d, and permission to obtain the children's school records, including ITBS/ITED results. For the child with diabetes, parents also signed permission to obtain the child's medical record, including a listing of HbA1c levels. The entire process took parents approximately 15 to 30 minutes. At the primary site where a research nurse was present in the clinic to enroll participants, 164 of 213 potential participants enrolled, resulting in a participation rate of 77%.

Collaborating Sites

At each of the other 4 sites, a list of all potential participants was obtained. Packets with the research information, forms, and a stamped return envelope were mailed to families. A reminder was sent approximately 3 weeks later. At the distant sites, where enrollment was conducted through mailed packets of information, the participation rate was 41%, with 80 of 195 potential participants enrolling.

Data Analysis

This study looked at both the current performance of children with diabetes and their performance over time in relation to 2 control groups: matched siblings and matched classmates. All available records were collected for each child and their matched sibling and matched classmate from school records and from Iowa Testing Programs records for grades 3 through 12. A cross-sectional approach was used to evaluate current performance. Statistical differences between groups were evaluated using matched t tests or McNemar's test for differences between related samples[33] as appropriate. Differences across time used longitudinal growth analysis. Growth curve characteristics were evaluated using hierarchical linear modeling (HLM).[34,35] This method provides an opportunity for controlled and uniform measurement of the exposure history of diabetes and achievement. It also provides information on individual patterns of change.[36]

Differences in achievement were analyzed using GPAs and ITBS/ITED standardized scores. For the ITBS/ITED scores, national percentile ranks (PRs) were transformed to a standard score with a mean of 100 and a standard deviation of 15. Students in this Midwestern state tend to score above the national average. The median national PR for this state equates to a standard score of 106 across grades 3 to 11 when transformed to a standard score.[37]

Data from the primary site were compared with data from the distant sites. There were no differences in current achievement scores, letter grades, or SES between groups at these sites for either children with diabetes or their siblings. Therefore, all subsequent analysis used data combined from all sites.

RESULTS

Hypothesis 1: Children With Type 1 Diabetes Will Demonstrate Deficits in Academic Performance and Behavior When Compared With Siblings or Classmate Control Subjects

First, current performance on the ITBS/ITED of children with diabetes who had a sibling in the study ($n = 110$) was compared with the current performance of their matched sibling (see Table 2). Comparisons were made between the total group of children with diabetes and their siblings and between subgroups of children with diabetes, based on age at onset, and their siblings. The age at onset dichotomy was defined as early-onset children with diabetes who presented before the age of 5 years and late-onset children who presented with diabetes at or after 5 years of age. The average age of onset for children in the early-onset group was 3.2 years (1.3) of age, in the late-onset group was 9.7 (2.9), and in the combined group was 8.0 (2.6). The mean grade for current testing of all children with diabetes, both early- and late-onset, was 8.1 (2.9), and the mean grade for their siblings was 7.9 (3.1). The mean current grade for children in the early-onset group was 7.1 (3.1) and for children in the late-onset group was 8.4 (2.7). It is interesting that the significant differences between all children with diabetes and their siblings were that the children with diabetes performed better in math and core total than their siblings. This same pattern was also noted for children with late-onset diabetes. Children with diabetes in the early-onset group performed slightly below children with late-onset in all areas, although no differences were statistically significant. Furthermore, this same pattern was seen in their siblings' scores.

Second, current performance on the ITBS/ITED of children with diabetes was compared with the current performance of their matched classmates (see Table 3). Comparisons were made between the total group of children with diabetes and their classmates and between subgroups of children with diabetes, based on age at onset, and their classmates. Children with diabetes and their matched classmates were at least 1 year postmatching, and the average time from matching was 4.4 years (2.8). Mean grade at current testing was 8.2 (2.8). Again, the children with diabetes performed at least as well as their classmates and were statistically better in reading than their classmates for the total group. Patterns of performance in both late- and early-onset groups were similar, unlike the patterns seen in the children with diabetes and their sibling comparison, in which the early-onset group tended to have lower mean scores than the late-onset group.

Third, children with diabetes were divided into 3 subgroups on the basis of metabolic control for the last year. Good metabolic control was defined as a mean HbA1c <8%, average metabolic control was defined as a mean HbA1c between 8% and 10%, and poor metabolic control was defined as a mean HbA1c >10%. These subgroupings resulted in slightly smaller numbers overall because not all children with diabetes had HbA1c data available in the year of the most recent achievement test. The most recent HbA1c and ITBS/ITED data, matched by grade, were used to form subgroups and to make comparisons between children with diabetes and their siblings (see Table 4) and their matched classmates (see Table 5). The performance of children with diabetes did not differ significantly from the performance of either their siblings or classmates at each level of control with 1 exception: children with diabetes who had average control performed better than their matched classmates in reading. It is interesting that poorer academic performance tended to occur in association with poor metabolic control and better performance with good control in all groups. These patterns were statistically significant in comparisons of good and poor metabolic control in children with diabetes matched with siblings for math ($P < .01$) and core total ($P < .03$).

Next, children with diabetes who had a sibling were compared with those siblings on other areas of academic performance. The 2 groups did not significantly differ on GPAs, repeated grades, or educational support. Children with diabetes had a mean GPA of 3.1 (0.8) compared with their matched siblings' mean GPA of 3.2 (0.7). Only 1 child with diabetes had repeated a grade, whereas 4 siblings had repeated a grade. Educational support, such as re-

TABLE 2. ITBS/ITED Current Performance: Children With Diabetes and Siblings*

	Number of Pairs	Children With Diabetes		Siblings		*P* Value
		Mean	Standard Deviation	Mean	Standard Deviation	
Reading						
All with diabetes	90	111.2	13.4	108.8	14.3	NS
Early-onset	16	104.9	9.2	107.2	11.9	NS
Late-onset	74	112.6	13.8	109.2	14.8	NS
Math						
All with diabetes	90	115.0	13.7	111.1	14.5	<.02
Early-onset	16	109.8	12.2	109.2	13.4	NS
Late-onset	74	116.1	13.8	111.5	14.8	<.02
Core total						
All with diabetes	86	113.9	14.0	110.5	14.9	<.04
Early-onset	16	108.1	11.3	108.8	13.9	NS
Late-onset	70	115.3	14.2	110.9	15.2	<.03

* Comparisons between children with diabetes and siblings using matched *t* tests. Early-onset is defined as onset of diabetes diagnosed before 5 years of age; late-onset is defined as onset of diabetes diagnosed at or after 5 years of age. NS indicates not significant.

TABLE 3. ITBS/ITED Current Performance: Children With Diabetes and Matched Classmates*

	Number of Pairs	Children With Diabetes		Classmates		*P* Value
		Mean	Standard Deviation	Mean	Standard Deviation	
Reading						
All with diabetes	186	108.9	14.5	106.8	13.1	<.04
Early-onset	37	109.2	13.3	106.8	12.3	NS
Late-onset	149	108.9	14.9	106.9	13.3	NS
Math						
All with diabetes	186	111.4	15.3	109.5	14.4	NS
Early-onset	37	110.3	12.5	110.5	10.7	NS
Late-onset	149	111.6	15.9	109.2	15.2	NS
Core total						
All with diabetes	185	110.0	15.6	108.6	13.8	NS
Early-onset	36	109.9	13.8	110.0	12.3	NS
Late-onset	149	110.5	16.0	108.2	14.2	NS

* Comparisons between children with diabetes and classmates using matched *t* tests. Early onset is defined as onset of diabetes diagnosed before 5 years of age; late onset is defined as onset of diabetes diagnosed at or after 5 years of age. NS indicates not significant.

TABLE 4. ITBS/ITED Current Performance Based on Metabolic Control: Children With Diabetes and Siblings

	Number of Pairs	Children With Diabetes		Siblings		*P* Value
		Mean	Standard Deviation	Mean	Standard Deviation	
Reading						
HbAlc <8	15	115.4	14.8	109.9	13.4	NS
HbAlc 8–10	45	111.5	12.8	110.0	14.3	NS
HbAlc >10	26	107.4	13.6	104.6	15.3	NS
Math						
HbAlc <8	16	121.8	10.1	116.9	11.7	NS
HbAlc 8–10	44	113.7	14.0	109.7	14.3	NS
HbAlc >10	26	109.4	14.7	108.4	15.5	NS
Core total						
HbAlc <8	15	119.5	12.0	112.0	13.0	NS
HbAlc 8–10	43	114.1	13.1	111.7	15.1	NS
HbAlc >10	25	108.8	14.5	105.9	15.3	NS

Good metabolic control = mean HbAlc <8 during the last year; average metabolic control = mean HbAlc 8 to 10 during the past year; poor metabolic control = mean HbAlc >10 during the past year. NS indicates not significant.

TABLE 5. ITBS/ITED Current Performance Based on Metabolic Control: Children With Diabetes and Matched Classmates

	Number of Pairs	Children With Diabetes		Classmates		*P* Value
		Mean	Standard Deviation	Mean	Standard Deviation	
Reading						
HbAlc <8	33	112.1	17.6	110.0	14.3	NS
HbAlc 8–10	91	110.5	13.2	107.4	12.3	<.02
HbAlc >10	54	105.9	13.1	104.9	14.2	NS
Math						
HbAlc <8	34	114.4	15.1	112.3	13.9	NS
HbAlc 8–10	91	111.3	14.8	109.7	13.9	NS
HbAlc >10	53	109.1	16.3	106.9	15.0	NS
Core total						
HbAlc >8	33	113.4	16.7	111.4	15.0	NS
HbAlc 8–10	92	111.1	13.8	109.5	13.2	NS
HbAlc >10	53	106.7	15.5	105.5	14.7	NS

Good metabolic control = mean HbAlc <8 during the past year; average metabolic control = mean HbAlc 8 to 10 during the past year; poor metabolic control = mean HbAlc >10 during the past year. NS indicates not significant.

source room assistance, was provided to 11 children with diabetes and 7 siblings. The only area in which the 2 groups differed significantly ($P < .02$) was in school absences: the children with diabetes missed more days per year, a mean absence rate of 7.3 (7.9), than their siblings, who had a mean absence rate of 5.3 (4.7).

Finally, behavior and emotional status, measured with the PBS-50d, were compared between children with diabetes and their siblings. The 2 groups did not differ on the 4 general factors of Aggression/Opposition ($P = .07$), Hyperactivity/Inattention ($P = .39$), Depression/Anxiety ($P = .70$), and Physical Complaints ($P = .09$). However, children with diabetes did differ significantly from their siblings on items that reflect compliance ($P < .01$), mood variability

($P < .01$), and fatigue ($P < .01$), but not learning ($P < .09$). These were the 4 areas included in the PBS-50d to reflect potential concerns for children with diabetes.

Hypothesis 2: Academic Performance in Children With Type 1 Diabetes Will Decline Slightly but Significantly Over Time, as the Physiologic Effects and the Psychological Burden of This Chronic Disease Influence Long-Term Achievement

In addition to current achievement analyses, which used only the most recent achievement data, an analysis of performance over time was conducted using all available student achievement data. HLM was used to estimate growth rates and possible differences between groups in growth trajectories. Two HLM analyses were conducted, 1 on children with diabetes and their siblings and 1 on children with diabetes and their matched classmates.

The initial HLM model is usually referred to as an unconditional model. It provides a set of baseline statistics for the mean intercept and growth rate that are useful in evaluating subsequent models. In this study, the mean intercept represents the average standard score of third graders. The growth estimate indicates the average amount of change in standard scores from year to year. In this study, if a student progressed at an average rate, then the "curve" for the standard scores across grades would be expected to be a horizontal line because the original achievement data were PRs. Students with consistent growth would be expected to retain a consistent ranking among the norm group across grades. The unconditional model mean intercept estimate for children with diabetes and their siblings at grade 3 was 108.97 with a standard error of 0.82. The mean growth rate was 0.40, which indicates that students gained an average of 0.40 of a standard score per grade. Both the average standard score and growth rate had large t statistics (132.55 and 3.23, respectively), indicating that both parameters are necessary to describe the mean growth trajectory. The unconditional model mean intercept estimate for the second group, children with diabetes and their matched classmates, was 108.83 with a standard error of 0.66. The mean growth rate was 0.23 of a standard score per grade. Both the average standard score and growth rate had large t statistics (163.91 and 2.21, respectively).

The reliability associated with the average standard score was 0.834 for the first group and 0.817 for the second group. This was evidence that there were individual differences in initial status, as expected. The reliability associated with the growth parameter was 0.403 and 0.385, respectively, which indicated that individual differences in the growth trajectories were too small and inconsistent to be detected.

The second HLM model introduced a group identifier to determine whether there were overall differences in growth trajectories between children with diabetes and their siblings or between children with diabetes and their matched classmates. When individual growth rates were averaged for each group, no statistically significant differences were found between groups. The t ratios for all predictors were between −1 and 1, indicating that initial status and growth rate were not strongly related to group membership and thus did not provide any additional explained variance. This is most clearly seen in Figs 1 and 2, which show the average achievement scores by grade. Only scores of children whose diabetes had been diagnosed before the time the test was taken were used in the analyses as seen in the different numbers of students included at each grade in Figs 1 and 2.

DISCUSSION

On standardized measures of academic achievement, children with type 1 diabetes performed at least as well as their siblings, who shared similar genetic backgrounds and home environments. Also, children who had been coping with diabetes for several years did at least as well in later academic performance as classmates who were matched on early academic achievement (typically at third grade) and then followed for an average of more than 4 years. The only statistically significant differences were in the direction of the children with diabetes performing slightly higher on some comparisons, but these differences were small and probably not clinically significant. The academic performance on the ITBS/ITED of all of the groups was in the normal range,

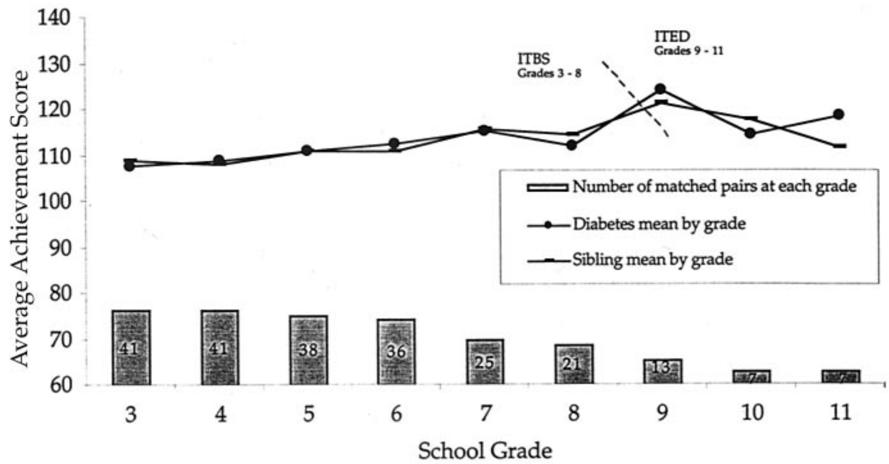

Fig 1. ITBS/ITED core total means: children with diabetes and their siblings.

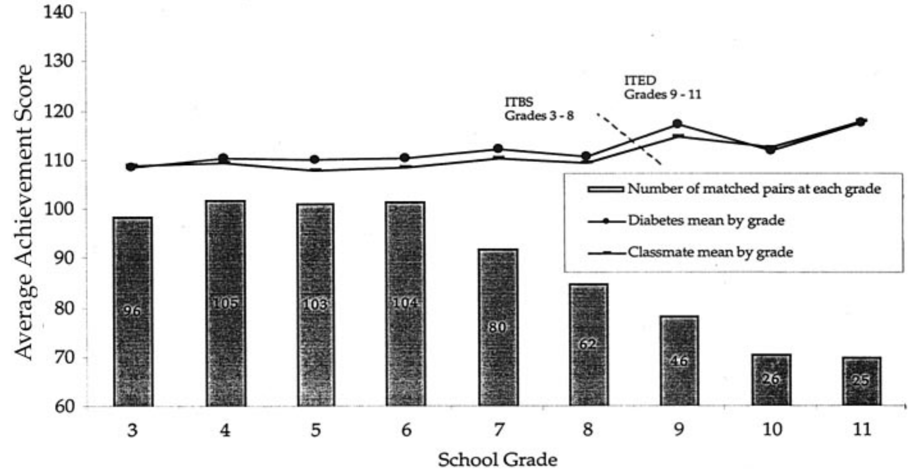

Fig 2. ITBS/ITED core total means: children with diabetes and their matched classmates.

generally within 1 standard deviation above the mean, which is typical of the academic performance of students in the state where the children in the study live. The absence of any significant differences between the academic growth curves of children with diabetes and either siblings or classmates indicates similar patterns of achievement over time.

Although early onset of diabetes was associated with slightly lower academic performance, children with early-onset type 1 diabetes did not differ significantly from sibling or classmate control subjects. Because children with diabetes were typically matched to classmate controls at third grade in the present study, early adverse effects of diabetes on learning in the early-onset group could have occurred before matching. However, if this were true, children with early-onset diabetes would be expected to perform more poorly overall than their siblings, which was not the case. There was also a trend toward higher achievement in children with better metabolic control, but again these children did not differ from their matched control subjects, particularly the sibling group. This pattern in children with diabetes may be more consistent with genetic or environmental impact on achievement rather than the effects of the disease. Instead of diabetes affecting achievement, it may be that brighter children with diabetes control their diabetes better. Children with diabetes did show significantly more school absences, as well as greater problems in compliance, mood variability, and fatigue, than did their siblings. The differences in both school attendance and behavior seemed to be specific to problems associated with this chronic disease and small enough to have minimal long-term effects on academic achievement in terms of either test scores or grades.

The results of this study suggest that the subtle neuropsychological deficits often documented in children with type 1 diabetes may not significantly limit the functional academic abilities of these children over time. There are several critical issues to consider in relating these findings to previous research. First, many previous studies used cross-sectional designs without an attempt to assess changes in learning over time. The only other study to report a longitudinal growth curve analysis of academic achievement[22] similarly did not find any differences in academic test scores between the children with diabetes and a matched control group. Although the children with diabetes in that study showed a decline in verbal abilities over time, so did the control subjects. The 2 groups differed only in classroom grades, with the diabetes group performing less well, which Kovacs et al[22] noted could have been attributable to the "psychosocial burden" of managing diabetes for many years rather than the direct neurocognitive effects of hypo- or hyperglycemia. Our group of children with diabetes did not differ in terms of grades or the need for special education services, which may mean that they have handled the burden of diabetes better than other groups in previous studies.

A second issue of concern is that ascertainment bias can influence the subject samples selected for study. It is difficult to enroll total populations of children with diabetes, and selecting any smaller subset introduces some degree of bias. This is certainly true of the current study, despite the fact that we were able to enroll more than three quarters of the potential subjects from our University Hospital diabetes clinic population, and our sample is one of the largest ever studied longitudinally. Smaller "convenience" samples in many previous studies were more prone to bias and were not always accurately matched to a large enough control sample, which can lead to spurious findings. Also, through the use of serial school test data in the present study, multiple hours of academic testing results could be obtained, in contrast to more limited academic screening typically done in clinic-based testing. This sample was clearly middle to upper-middle class, which may protect children from the subtle neuropsychological impairments that have been noted in some children with diabetes. However, because our sample is relatively homogeneous, it allows us to assess better the direct effects of the disease and to minimize confounding by SES factors.

It is important to recognize that the lack of achievement differences for groups of children with diabetes does not suggest that all of the individual children in the sample are free of learning problems. For example, Rovet and colleagues[14,38] reported no differences in neuropsychologic abilities, academic achievement, and socioemotional status when comparing 103 children and adolescents with diabetes to a control group of 100 healthy children and adolescents. There was also no decline in achievement over time when a subset of 16 of these children were followed for 7 years. When the subjects were grouped by seizure history, however, those with seizures scored significantly lower on tests of memory, attention, perception, and motor skills. In the current study, we were not able to assess reliably the seizure history in the children with diabetes; thus, we cannot exclude the possibility that a small subset of these children could be experiencing neurocognitive problems secondary to hypoglycemic seizures. Fortunately, these problems would have to be infrequent and subtle or they would have been reflected in larger between-group differences in the data. It is important to recognize, though, that we did not perform comprehensive neuropsychological assessments in the current study, and global achievement tests such as the ITBS/ITED may not be sensitive to subtle neurocognitive effects. If diabetes produces deficits in attention or executive functioning, then learning could be affected even if basic academic skills are intact. However, we found no differences in either school grades or parent ratings of attention in this study. It is important to note that the children in this study were on conventional as opposed to intensive diabetes management. Intensive therapy may result in more hypoglycemic episodes, with a possible increase in neuropsychological deficits, which in turn may affect academic skills.[39]

Finally, the fact that there has been very little consistency in the type of cognitive deficits associated with type 1 diabetes in previous studies makes it difficult to hypothesize a precise mechanism for any presumed neurocognitive effects.[17] It could be argued that varying blood sugar levels accentuate whatever cognitive weaknesses may already be present in a particular child, which might lead to verbal deficits in some children and spatial or motor deficits in others. It can also be argued that fluctuating blood sugar levels affect attention and speed of processing to an extent that other types of cognitive effects may be seen as secondary effects of difficulties in glycemic control. It is critical to recognize, however, that even if some specific types of neurocognitive effects can be demonstrated in some populations, these effects may be too subtle to produce significant changes in long-term academic performance. In fact, recent studies[38–40] implicated hypoglycemic seizures as the primary risk factor associated with diabetes that seems to have consistent adverse effects on cognition.

CONCLUSION

This study reinforces the conclusion of Ryan[17] that major long-term cognitive deficits in children with type 1 diabetes, with only a few exceptions (eg, in association with hypoglycemic seizures), cannot be attributed to the effects of diabetes. The subtle neurocognitive impairments that have been documented in some children with diabetes at some ages may not necessarily produce measurable decrements in academic performance, even over time. These findings should provide reassurance to children with diabetes and their families, the educators who teach them, and the health professionals who care for them. There is still a need, however, to monitor carefully children who are receiving intensive treatment to prevent seizures and to ensure that increased episodes of hypoglycemia (especially if associated with seizures or coma) are not adversely affecting learning.

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REFERENCES

1. Johnson SB. Diabetes mellitus in childhood. In: Routh DK, ed. *Handbook of Pediatric Psychology*. New York, NY: Guilford Press; 1988:9–31
2. Onkamo P, Vaananen S, Karvonen M, Tuomilehto J. Worldwide increase in incidence of type 1 diabetes: analysis of the data on published incidence trends. *Diabetologia.* 1999;42:1395–1403
3. Ack M, Miller I, Weil WB. Intelligence of children with diabetes mellitus. *Pediatrics.* 1961;28:764–770
4. Brown DG. The development of diabetic children, with special reference to mental and personality comparisons. *Child Dev*. 1938;9:175–184
5. Hagen JW, Barclay CR, Anderson BJ, et al. Intellective functioning and strategy use in children with insulin-dependent diabetes mellitus. *Child Dev*. 1990;61:1714–1727
6. Northam EA, Anderson PJ, Werther GA, Warne GL, Adler RG, Andrewes D. Neuropsychological complications of IDDM in children 2 years after disease onset. *Diabetes Care.* 1998;21:379–384
7. Holmes CS, Richman LC. Cognitive profiles of children with insulin-dependent diabetes. *Dev Behav Pediatr*. 1985;6:323–326
8. Northam E, Anderson P, Werther G, Adler R, Andrewes D. Neuropsychological complications of insulin dependent diabetes in children. *Child Neuropsychol*. 1995;1:74–87
9. Ryan C, Vega A, Longstreet C, Drash A. Neuropsychological changes in adolescents with insulin-dependent diabetes. *J Consult Clin Psychol*. 1984;52:335–342
10. Ryan CM, Vega A, Drash A. Cognitive deficits in adolescents who developed diabetes early in life. *Pediatrics.* 1985;75:921–927
11. Rovet J, Ehrlich R, Hoppe M. Specific intellectual deficits in children with early onset diabetes mellitus. *Child Dev*. 1988;59:226–234
12. Ryan CM, Longstreet C, Morrow L. The effects of diabetes mellitus on the school attendance and school achievement of adolescents. *Child Care Health Dev*. 1985;11:229–240
13. Golden M, Ingersoll GM, Brack CJ, Russell BA, Wright JC, Huberty TJ. Longitudinal relationship of asymptotic hypoglycemia to cognitive function in type 1 diabetes. *Diabetes Care.* 1989;12:89–93
14. Rovet J, Alvarez, M. Attentional functioning in children and adolescents with IDDM. *Diabetes Care.* 1997;20:803–810
15. Northam EA, Anderson PJ, Werther GA, Warne GL, Andrewes D. Predictors of change in the neuropsychological profiles of children with type 1 diabetes 2 years after disease onset. *Diabetes Care.* 1999;22:1438–1444
16. Ryan C. Neurobehavioral complications of type I diabetes: examination of possible risk factors. *Diabetes Care.* 1988;11:86–93
17. Ryan C. Effects of diabetes mellitus on neuropsychological functioning: a lifespan perspective. *Semin Clin Neuropsychol*. 1997;2:4–14
18. Weil WB, Ack M. School achievement in juvenile diabetes mellitus. *Diabetes.* 1964;13:303–306
19. Fowler MG, Johnson MP, Atkinson SS. School achievement and absence in children with chronic health conditions. *J Pediatr*. 1985;106:683–687
20. Gath A, Smith MA, Baum JD. Emotional, behavioral, and educational disorders in diabetic children. *Arch Dis Child*. 1980;55:371–375
21. Holmes CS, Dunlap WS, Chen RS, Cornwell JM. Gender differences in

the learning status of diabetic children. *J Consult Clin Psychol*. 1992;60: 698–704
22. Kovacs M, Goldston D, Iyengar S. Intellectual development and academic performance of children with insulin-dependent mellitus: a longitudinal study. *Dev Psychol*. 1992;28:676–684
23. Kovacs M, Ryan C, Obrosky DS. Verbal intellectual and visual memory performance of youths with childhood-onset insulin-dependent diabetes mellitus. *J Pediatr Psychol*. 1994;19:475–483
24. Holmes CS, Respess D, Greer T, Frentz J. Behavior problems in children with diabetes: disentangling possible scoring confounds on the child behavior checklist. *J Pediatr Psychol*. 1998;23:179–185
25. Grey M, Cameron ME, Lipman TH, Thurber FW. Psychosocial status of children with diabetes in the first 2 years after diagnosis. *Diabetes Care.* 1995;18:1330–1336
26. Northam E, Anderson P, Adler R, Werther G, Warne G. Psychosocial and family functioning in children with insulin-dependent diabetes at diagnosis and one year later. *J Pediatr Psychol*. 1996;21:699–717
27. Hollingshead A. *Two-Factor Index of Social Position*. New Haven, CT: Yale University Department of Sociology; 1965
28. Hoover HD, Hieronymous DA, Frisbie DA, Dunbar SB. *Iowa Tests of Basic Skills Complete Battery, ITBS Form K.* Chicago, IL: Riverside; 1993
29. Feldt LS, Forsyth RA, Ansley TN, Alnot SD. *Iowa Tests of Educational Development*. Chicago, IL: Riverside; 1993
30. *Technical Summary I. Riverside 2000.* Chicago, IL: Riverside; 1994
31. Lindgren SD, Koeppl GK. Assessing child behavior in a medical setting: development of the Pediatric Behavior Scale. In: Prinz RJ, ed. *Advances in Behavioral Assessment of Children and Families, III*. Greenwich, CT: JAI; 1987:57–90
32. American Diabetes Association. Implications of the Diabetes Control and Complications Trial. *Diabetes Care.* 1993;16:1517–1520
33. McNemar Q. *Psychological Statistics.* 4th ed. New York, NY: John Wiley; 1969
34. Bryk AS, Raudenbush SW. *Hierarchical Linear Models: Applications and Data Analysis Methods.* Newbury Park, CA: Sage Publications; 1992
35. Raudenbush S, Bryk A, Cheang YF, Congdon R. *HLM5: Hierarchical Linear and Nonlinear Modeling.* Lincolnwood, IL: Scientific Software International; 2000
36. Ware JH. Linear models for the analysis of longitudinal studies. *Am Stat* 1985;39:95–101
37. Iowa Testing Program. *Score Reports and Norms.* Iowa City, IA: Iowa Testing Programs; 2000
38. Rovet JF, Ehrlich RM. The effect of hypoglycemic seizures on cognitive function in children with diabetes: a 7-year prospective study. *J Pediatr*. 1999;134:503–506
39. Hershey T, Bhargava N, Sadler M, White NH, Craft S. Conventional versus intensive diabetes therapy in children with type 1 diabetes. *Diabetes Care.* 1999;22:1318–1324
40. Kaufman FR, Epport K, Engilman R, Halvorson M. Neurocognitive functioning in children diagnosed with diabetes before age 10 years. *J Diabetes Complications.* 1999;13:31–38

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