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Neurocognitive functioning in children with type-1 diabetes with and without episodes of severe hypoglycaemia

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Previous studies have shown that recurrent severe hypoglycaemia can cause long-term cognitive impairment in children with type-1 diabetes, but the results are controversial, possibly due to the heterogeneity of samples and lack of comprehensive neuropsychological assessments of children. The aim of this study was to assess the effects of diabetes and severe hypoglycaemia on the neurocognitive functioning of children with a standardized, wide age-range neuropsychological test battery designed for the assessment of children. Eleven children with diabetes and a history of severe hypoglycaemia, 10 children with diabetes without a history of severe hypoglycaemia, and 10 healthy control children (a total of 31 children: 14 males and 17 females, age range 5 years 6 months to 11 years 11 months, mean 9 years 4 months, SD 1 year 11 months) were studied using the Wechsler Intelligence Scale for Children–Revised (WISC-R) and the NEPSY, a Developmental Neuropsychological Assessment. The NEPSY assessed development in attention and executive functions, language, sensorimotor functions, visuospatial processing, and learning and memory. Children with a history of severe hypoglycaemia had more neuropsychological impairments, more learning difficulties (as reported by parents), and needed more part-time special education than those in the other groups. Significant differences were found in verbal short-term memory and phonological processing. Results suggest that severe hypoglycaemia is a risk factor for learning due to deficits in auditory–verbal functioning.

Type-1 (insulin-dependent) diabetes mellitus is a chronic metabolic disorder caused by an autoimmune destructive process of the pancreatic beta cells, leading to hyperglycaemia and to the need for insulin replacement therapy. The geographical incidence varies considerably throughout the world, with highest rate in Finland (45 per 100 000 children below 15 years of age per year; Tuomilehto et al. 1999).

One of the main goals of diabetes management is to achieve near-normoglycaemia to prevent or to minimize the long-term complications of diabetes (retinopathy, nephropathy, and neuropathy). However, attempts towards near-normoglycaemia can lead to an increasing incidence of hypoglycemic episodes, which are the most common acute complications of insulin therapy.

For descriptive and clinical purposes, hypoglycaemia in children can be divided into four categories: (1) asymptomatic (biochemical), (2) mild symptomatic, (3) moderate symptomatic, and (4) severe hypoglycaemia. In mild symptomatic hypoglycaemia, the patients are able to detect and treat the hypoglycaemia by themselves. In moderate hypoglycaemia, the aid of another person is needed. Hypoglycaemia is severe when the patient is unconscious, and/or has convulsions. Virtually no hypoglycaemia occurring in children under 6 years can be classified as mild as young children are rarely able to treat themselves. Annually, 5–10% of children with type-1 diabetes mellitus experience severe hypoglycaemia leading to unconsciousness. They may experience mild symptomatic or asymptomatic hypoglycaemic episodes weekly (Åman et al. 1989, Barkai et al. 1998).

It has been noticed that recurrent severe hypoglycaemia can cause long-term cognitive impairment in children with type-1 diabetes (Rovet et al. 1987, Bjørgaas et al. 1997, Rovet and Ehrlich 1999), but valid reports in which such correlations have not been found also exist (Ryan et al. 1985, Northam et al. 1992). Deficits in verbal abilities (Rovet and Alvarez 1997), spatial abilities (Rovet 2000), attention (Bjørgaas et al. 1997, Rovet and Alvarez 1997), and short-term memory (Rovet and Ehrlich 1999) have been reported in connection with episodes of severe hypoglycaemia. The vast majority of the evidence with regard to the long-term effects of hypoglycaemia on neurocognitive performance is based on adults with long-standing diabetes and the results are controversial (Rovet 2000).

Studies on the effects of severe hypoglycaemia in children with diabetes have been made using small sample sizes (Rovet et al. 1987, Bjørgaas et al. 1997, Kaufman et al. 1999). Recently, Northam and coworkers (1999, 2001) published a prospective study with a large and representative cohort. The variety of tests used to assess different neurocognitive domains make it difficult to compare results between studies. Wide age-ranges within studies have also led to problems in test selection. Many of the neuropsychological tests used have either been originally developed for adults (e.g. Wisconsin Card Sorting Test; Berg 1948) or are experimental tests, thereby rendering evaluation of the clinical relevance of the results difficult.

In this controlled study we assessed the effects of diabetes and severe hypoglycaemia on neurocognitive functioning in children with a comprehensive neuropsychological test battery, including standardized normative values for every age group.

Method

PARTICIPANTS

The study population consisted of 21 children with type-1 diabetes mellitus and 10 healthy children (Table I). The ages of the children ranged from 5 years 6 months to 11 years 11 months and the duration of diabetes ranged from 1 year 9 months to 9 years 7 months. The children with diabetes were outpatients at Kymenlaakso Central Hospital in Finland. Of the children with diabetes, 11 had experienced at least one episode of severe hypoglycaemia (D+H group), defined as unconsciousness and/or convulsions associated with blood glucose concentration <3mmol/L or with prompt response to the administration of glucagon or intravenous glucose. The other 10 children with diabetes had never experienced severe hypoglycaemia (D–H group). The unaffected children served as controls (C group). They consisted of volunteers from the children of hospital staff and children from a local sports club.

All children at Kymenlaakso Central Hospital outpatient clinic who had experienced severe hypoglycaemia and met the criteria for prepubescence (Tanner Stage 1; Tanner 1962) and had normal milestones in psychomotor development (evaluated at well-child clinic and by a paediatrician at the hospital) were included in the study. The D+H group was matched with the D–H and C groups for sex, age, and parents' educational level. Parents' educational level was categorized as 1, compulsory 9-year education only; 2, vocational education or similar; 3, college education or similar; and 4, university education. The clinical data on severe hypoglycaemia were confirmed both by interviewing children and their families and by reviewing hospital records. Of the children with hypoglycaemia, four had experienced 1 episode, four had 2 episodes, two had 3 episodes, and one child had 4 episodes of severe hypoglycaemia. The episodes had occurred 9 months to 7 years (median 4 years) before the study. The two diabetic groups did not differ in recent metabolic control, defined as HbA1c-value, or in prevalence and severity of initial ketoacidosis, defined as serum pH<7.3 (see Table I). None had been unconscious during ketoacidosis, and none of the children had experienced later ketoacidosis. The two diabetes groups differed in age at diagnosis and duration of illness. Age at diagnosis was younger and duration of diabetes was longer in the D+H group than in the D–H group (see Table I). All the children had normal psychomotor development and had no history of intrauterine or perinatal problems, other neurological disorders, nor trauma. No one had experienced any psychological crises. All children were in ordinary elementary schools except for four who were in preschool.

NEUROPSYCHOLOGICAL ASSESSMENT

The Finnish version of the Wechsler Intelligence Scale for Children–Revised (WISC-R; Wechsler 1984) was used to assess general intelligence in the children aged 6 years and older. A 5-year-old child in the D–H group received the Finnish version of the Wechsler Preschool and Primary Scale of Intelligence–Revised (WPPSI-R; Wechsler 1995). All the verbal subtests (Information, Similarities, Arithmetic, Vocabulary, and Comprehension) were administered and they formed the Verbal IQ score. Performance IQ was formed from the Picture Completion, Block Design, Object Assembly, and Coding subtests (Picture Completion, Block Design, and Object Assembly in WPPSI-R). The IQ scores (Full-Scale, Verbal, and Performance IQ) have a mean of 100 (SD 15) and for the individual subtests the mean is 10 (SD 3). The Digit span forward assessed verbal short-term memory and was included in the neuropsychological domain of Memory and learning.

The NEPSY, a Developmental Neuropsychological Assessment (Korkman et al. 1997) is a neuropsychological test for children 3 to 12 years of age. The Finnish version consists of 30 neuropsychological subtests designed to assess neuropsychological development in five functional domains: Attention/Executive functions, Language, Sensorimotor functions, Visuospatial processing, and Memory and learning. The subtests of the Finnish version correspond to the English version of the NEPSY (Korkman et al. 1998). The subtests have been standardized on a single sample of children (Korkman 2000). Each age group has its own standardized normative values where the mean standard score is 10 (SD 3). Of the 30 NEPSY subtests, 16 were administered (Table II). The selected subtests

Table I: Characteristics of diabetes and hypoglycaemia (D+H), diabetes without hypoglycaemia (D–H), and control groups

Characteristics	*Groups*			*Significant group differences*
	D+H (n=11)	*D–H (n=10)*	*Control (n=10)*	
Sex, *n*	5 M, 6 F	4 M, 6 F	5 M, 5 F	
Age, y; mean (SD)	9.55 (2.19)	9.10 (1.92)	9.23 (1.79)	
Parents' education[a], mean (SD)	2.09 (0.83)	2.40 (0.84)	2.90 (0.99)	
Age at diagnosis, y; mean (SD)	3.32 (1.45)	5.40 (2.38)		$t=-2.45(18)$[f]
Duration of diabetes, y; mean (SD)	6.16 (2.52)	3.70 (1.63)		$t=2.67(18)$[f]
HbA1c, %[b]; mean (SD)	8.3 (1.9)	8.4 (2.0)		
Initial ketoacidosis, *n*	2	3		
Learning difficulties[c], *n*	5[e]	2[e]	0[e]	$\chi^2=7.33(2)$[f]
Special education, *n*	5[e]	2[e]	0[e]	$\chi^2=7.33(2)$[f]
Neuropsychological impairment[d], *n*	7	3	0	$\chi^2=9.74(2)$[f]

[a]Parents' education was categorized as: 1, compulsory 9-year education only; 2, vocational education or similar; 3, college education or similar; and 4, university education; [b]DCA 2000 Analyzer (Bayer Corporation, Elkhart, IN, USA), reference limit 4–6.2%; [c]Learning difficulties as reported by parents; [d]Indicated as standard score <4 in any of the NEPSY subtests (Korkman et al. 1997); [e]$n=9$; [f]$p<0.05$.

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were mainly core subtests of the domains. Picture perception and Picture recognition subtests were used in order to obtain information about the visuospatial memory of the children with diabetes. The tests were administered in the same order to all the children.

PROCEDURE

All the children were assessed by the same psychologist over two or three sessions, with each session lasting 45 to 60 minutes. Between sessions there was a break. According to the wishes of the child and the parents, the sessions were scheduled for the same day or for different days within a 2-week period. The examiner was not informed which of the two diabetes groups the child belonged to. After the evaluation of the children with diabetes the control group was assessed. The blood glucose level of the children with diabetes was measured before each assessment session. None of the children had symptoms of hypoglycaemia or blood glucose value <3mmol/L at the time of assessment.

At the beginning of the assessment a structured interview on the child's cognitive development, learning, and social relationships was administered to the parents. The parents were asked if the child had learning difficulties in reading, spelling, or mathematics or had received part-time special education at school. Informed consent was obtained from the parents. The ethics committee of the hospital approved the study.

Table II: Description of NEPSY subtests (Finnish version; Korkman et al. 1997)

Domain	*Subtest*	*Description*
Attention/Executive functions	Tower	Assesses planning, monitoring, and problem solving. The child has to arrange 3 balls on 3 pegs in a prescribed number of moves and time limit.
	Auditory attention and Response set	Assesses vigilance, selective auditory attention, and ability to shift set. The child learns to respond to certain word in Part A, and has to shift set and respond to contrasting stimuli in Part B.
	Visual attention	Assesses the speed and accuracy of visual search.
Language	Phonological processing	Assesses the ability to process the phonology of words. The child has to identify words from segments or create a new word by omitting a word segment.
	Comprehension of instructions	Assesses the ability to process and respond to verbal instructions. Requires understanding of concepts and syntactic features.
	Speeded naming	Assesses the ability to access and produce familiar words rapidly. The child has to name quickly the size, color and shape of the object. Time and errors are recorded.
	Verbal fluency	Assesses the ability to generate words according to semantic and phonemic categories.
Sensorimotor functions	Fingertip tapping	Assesses finger dexterity and psychomotor speed. The child taps the index finger against the thumb 30 times. In the second part the child taps the fingers sequentially against the thumb. The score measures the time taken.
	Visuomotor precision	Assesses fine motor skills and hand-eye coordination. The child draws a line inside a track without crossing over the boundaries. The score measures both errors and the time taken.
	Finger discrimination	Assesses tactile perception. Without the aid of vision, the child identifies which of his fingers the examiner touches.
Visuospatial processing	Design copying	Assesses visuomotor integration and visuospatial skills. The child copies two-dimensional figures.
	Arrows	Assesses the ability to judge the direction, angularity and orientation of lines. The child is asked which two of eight arrows hit the target.
	Picture perception	Assesses visual recognition. The child is presented with three photos of an object, with 3s for each photo. The first photo is not sharply focused, the second is sharper and the third is the sharpest. The child is asked to name the object as soon as s/he recognizes it. (This test is not in the English version of NEPSY.)
Memory and learning	Picture recognition	Assesses visual and visuospatial memory. The child is asked to select the photo he has seen in the previous subtest from among four photos of similar objects. (This test is not in the English version of NEPSY).
	Memory for names	Assesses pair-associative memory for visual and verbal information. The child learns the names of the children seen in eight pictures. The pictures are presented three times, and 30min after the last presentation the child is asked to name the children in the pictures again.
	List learning	Assesses verbal learning. A 15-item word list is presented over five trials. An interference list is administered and recalled once, and the child is then asked to repeat the first list. Delayed recall time is after 30min. (This subtest was administered only to children who were 7 years and older.)

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STATISTICAL ANALYSIS

Multivariate analysis of variance was used to determine group effects on general intelligence and on the neuropsychological domains. Parents' education was entered as a covariate. The data of the two diabetes groups were analyzed using parents' education, age at diagnosis, and duration of diabetes as covariates. Univariate ANOVA models were used to determine group differences in the IQ measures and in the individual subtests. Pairwise comparisons were further analyzed by Tukey's HSD test. Cross-tabulations with the χ^2 test were used to determine differences between the groups in the dichotomous variables (e.g. learning difficulties, need for special education).

Results

Significant differences were found in the learning difficulties reported by parents ($\chi^2=7.33(2), p<0.05$) and need for part-time special education ($\chi^2=7.33(2), p<0.05$). Most learning difficulties and special education needs were reported in the D+H group, indicating that the children who had experienced severe hypoglycaemia had more learning difficulties in reading, spelling, and mathematics (see Table I).

Because previous studies have not found conclusive evidence on the clinical significance and quality of neurocognitive impairments in children with diabetes, we took the evaluation of clinically significant neurocognitive impairments as our first task. A significant neuropsychological

Table III: Test scores in diabetes and hypoglycaemia (D+H), diabetes without hypoglycaemia (D–H), and control groups. Values are mean standard scores (SD)

Tests/subtests	*Groups*			*Significant group differences*
	D+H (n=11)	*D–H (n=10)*	*Control (n=10)*	
WISC-R				
Information	7.36 (2.34)	9.60 (3.44)	8.50 (2.01)	
Similarities	9.45 (1.81)	9.80 (3.29)	9.50 (1.65)	
Arithmetic	9.18 (2.32)	10.40 (1.58)	10.80 (1.93)	
Vocabulary	6.36 (2.98)	8.90 (3.84)	9.30 (2.87)	
Comprehension	7.91 (2.43)	8.80 (2.82)	8.60 (2.59)	
Picture completion	8.45 (2.46)	10.00 (3.20)	9.80 (2.82)	
Block design	11.18 (1.94)	11.50 (2.80)	12.40 (3.27)	
Object assembly	10.55 (2.38)	11.10 (3.38)	11.20 (2.04)	
Coding	11.18 (2.23)	10.56 (3.13)	11.00 (2.75)	
Verbal IQ[a]	87.91 (10.05)	96.30 (14.93)	95.40 (9.86)	
Performance IQ[a]	102.09 (12.73)	106.10 (16.58)	107.20 (14.36)	
Full-scale IQ[a]	93.55 (10.13)	101.00 (15.58)	101.00 (10.58)	
NEPSY				
Attention/Executive functions				
Tower	12.27 (1.90)	10.60 (2.84)	13.50 (2.07)	D–H<C[c]
Auditory attention	9.27 (4.27)	11.80 (2.57)	11.10 (2.33)	
Visual attention	10.82 (1.25)	10.90 (3.70)	10.90 (2.42)	
Language				
Phonological processes	7.45 (3.70)	9.00 (2.62)	11.10 (2.38)	D+H<C[c]
Comprehension	7.00 (2.61)	8.90 (4.09)	8.80 (3.26)	
Speeded naming	9.18 (2.86)	11.30 (2.11)	10.10 (2.13)	
Verbal fluency	8.36 (3.91)	7.90 (4.84)	11.90 (2.73)	
Sensorimotor functions				
Fingertip tapping	12.09 (1.81)	12.80 (1.14)	12.60 (1.58)	
Visuomotor precision	11.00 (2.65)	10.90 (3.78)	11.60 (4.33)	
Finger discrimination	10.09 (2.63)	10.30 (2.98)	11.40 (1.84)	
Visuospatial processing				
Design copying	11.45 (2.21)	11.70 (2.63)	11.70 (1.89)	
Arrows	11.18 (2.71)	11.20 (1.23)	12.00 (2.49)	
Picture perception	9.73 (3.00)	12.40 (2.07)	11.00 (2.87)	
Memory and learning				
Picture recognition	11.09 (3.18)	10.40 (3.03)	10.90 (2.42)	
Memory for names	8.82 (2.86)	9.70 (3.27)	11.00 (3.30)	
List learning	9.44 (2.46)	10.22 (3.35)	11.57 (4.69)	
Digit span forward[b]	4.73 (0.79)	4.60 (0.52)	5.80 (0.92)	D+H<C[d] D–H<C[d]

[a]Mean 100, SD 15, in subtests, standard score mean 10, SD 3; [b]raw score; [c]$p<0.05$; [d]$p<0.01$.

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impairment is considered to exist when a person scores 2SD below the neuropsychological test mean (standard score <4). On the basis of the volume of neuropsychological impairment in the groups, we counted as having impairment those children who had at least one standard score <4. In the D+H group seven of 11 and in the D–H group three of 10 had significant neuropsychological impairments in at least one area of functioning, mainly in language and executive functions. None of the children in the control group had any neuropsychological deficits (see Table I). The between-group difference was significant ($\chi^2=9.74(2), p<0.05$).

The test scores in the D+H, D–H, and C groups are displayed in Table III. The data were analyzed with multivariate analyses of variance within the Wechsler tests and neuropsychological domains. Due to the small size of the sample, the power of the analysis was not sufficient to detect small differences. There were almost significant group effects in the neuropsychological domains of Memory and learning ($p=0.09$), Attention/Executive functions ($p=0.12$), and Language ($p=0.15$). Parents' education was not a significant covariate in any of the analyses.

In the neuropsychological subtests assessing Memory and learning a significant difference was found in the Digit span forward ($F=7.6$ (2, 28), $p<0.01$). Digit span forward was exceptionally short in both diabetes groups (D+H mean 4.73 digits [SD 0.79, $p<0.01$] and D–H mean 4.6 [SD 0.52, $p<0.01$]) when compared with the control group (mean 5.80 [SD 0.92]). In the neuropsychological subtests assessing language functions a significant difference was found in Phonological processes ($F=3.92$ (2, 28), $p<0.05$). The D+H group had lower standard scores than control children ($p<0.05$). In the neuropsychological subtests assessing Attention/Executive functions, Visuospatial and Sensorimotor functions, all three groups scored near or over the standard means of the subtests, indicating high-level abilities. Group differences were found in the Tower subtest assessing planning and executive processes ($F=4.04$ (2, 28), $p<0.05$). A significant difference was found between the D–H and C groups ($p<0.05$). No statistical difference was found in the Wechsler subtests. Verbal IQ in the D+H group was 87.9, in the D–H group 96.3, and in the control group 95.4, but the differences did not reach statistical significance.

Because the two diabetes groups differed in age at diagnosis and duration of illness, comparison within the diabetes groups were made using these variables and parents' education as covariates. A significant group effect ($F=4.43$ (3, 14), $p<0.05$) was found in attention and executive functions. Pairwise comparisons revealed significant differences in the Tower subtest ($p<0.05$), where the D–H group had lower scores than the D+H group, and in Auditive attention ($p<0.05$), where the D+H group performed more poorly than the D–H group. Age at diagnosis ($p<0.05$) and duration of diabetes ($p<0.01$) were significant covariates in the Auditive attention subtest. There was no significant group effect in any of the other neuropsychological domains nor in intelligence.

Discussion

The aim of the study was to assess the effects of diabetes and severe hypoglycaemia on neurocognitive functioning in children. We used a comprehensive, well standardized, and validated, wide age-range neuropsychological test in order to assess a variety of cognitive domains. By means of the NEPSY, it is possible to study both basic and complex aspects of neurocognitive functioning with subtests appropriate across wide age groups, thereby obtaining information on the clinical relevance of neurocognitive deficits when compared with age expectations (Korkman et al. 1998). A comprehensive neuropsychological assessment can explain a behavioural outcome (e.g. learning difficulty) by showing the deficits in basic function (e.g. phonological processing).

In this study, the children with diabetes who had experienced severe hypoglycaemia had significantly more neuropsychological deficits and learning difficulty, and they needed more special education than the healthy children or the children with diabetes but without a history of severe hypoglycaemia. The clinical significance of cognitive impairments in children with diabetes has not been fully recognized in previous studies. Significant differences were found in verbal short-term memory and phonological processing skills between the children who had experienced severe hypoglycaemia and the healthy children. Other studies have also reported a relation between poorer short-term memory and severe hypoglycaemia (Kaufman et al. 1999, Northam et al. 1999, Rovet and Ehrlich 1999). Phonological processing skills have not been assessed comprehensively in previous studies. Deficits in auditory–verbal functions, as found in our study, have an influence on the development of verbal skills. They may partly explain the lower verbal intelligence in children with a history of severe hypoglycaemia found in the prospective studies by Rovet and Ehrlich (1999) and Northam and colleagues (2001).

The frontal and temporal regions, particularly in the left hemisphere, are involved in language, memory, and attentional processes. Auer and Siesjo (1988) and Chalmers and colleagues (1991) found that abnormal blood glucose levels in particular affect the frontal and temporal regions of the brain, especially the hippocampus (Auer 1986). In cerebral blood flow studies hypoglycaemia has been shown to have an asymmetrical effect with a greater reduction of left- versus right-hemisphere profusion (Jarjour et al. 1995).

The brains of infants appear to have an increased vulnerability to hypoglycaemia (Harwoth and Coodin 1960). Preterm infants born small for gestational age (Lucas et al. 1988), infants of mothers with diabetes (Schwartz and Teramo 2000), and infants with persistent hyperinsulinemic hypoglycaemia (Cresto et al. 1998) are most at risk. An adverse neurodevelopmental outcome can be seen even after moderate neonatal hypoglycaemia (Lucas et al. 1988), and prolonged or repeated episodes of profound neonatal hypoglycaemia may lead to severe learning disability* and epilepsy (Menni et al. 2001). In contrast to these patients, children with diabetes are usually older and recover from severe hypoglycaemic attacks without permanent major neurological deficits (Tupola et al. 1998). However, transient hemiplegia after severe hypoglycaemia has been described in children with diabetes (Lala et al. 1989, Wayne et al. 1990). The mechanism of this neurological deficit remains unclear.

In our study, the neurocognitive functioning of the children with diabetes and without an experience of severe hypoglycaemia was less affected than that of those with recurrent severe hypoglycaemia. However, they too had slightly poorer auditory–verbal skills than the unaffected

*US usage: mental retardation.

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children. In addition, they differed in a task requiring executive processes. Thus, diabetes can be associated with subtle, diffuse deficits in the child's performance. The explanation could lie in the mild symptomatic or asymptomatic hypoglycaemic episodes which all children with diabetes experience. Such episodes cause transient cognitive deficits, especially in planning and cognitive flexibility, sustained attention, and reaction time (Ryan et al. 1990) and, cumulatively, may have a negative effect on the child's performance.

Minor problems in neurocognitive functioning may cause learning difficulties at school. Ryan (1988) reported poorer school achievement among children with diabetes, especially in reading and spelling. In our study, the children with diabetes and especially those who had experienced severe hypoglycaemia had more learning difficulties reported by parents and needed more part-time special education than the unaffected children. A limitation of the study is that teachers' reports were not obtained. In the literature, there is no consensus regarding the link between specific learning disorders and diabetes. When compared with other groups of children with chronic illnesses, children with diabetes perform more poorly at school and surpass only those children with a neurological illness e.g. epilepsy (Fowler et al. 1985). Deficits in neurocognitive functioning apart, other reasons can be adduced to explain the poorer school achievement of children with diabetes. They may be more frequently absent from school, which can affect school performance. Mild hypoglycaemic episodes have an influence on attention (Ryan et al. 1990, Gschwend et al. 1995), psychomotor speed and memory (Reich et al. 1990), and learning in the classroom is not always effective. It is likely that teachers are not always aware of hypoglycaemia-induced cognitive deficits, and this may also influence performance at school.

The limitations of the current study are acknowledged. We have used a small sample, and this restricts the generalizability of the results. Nevertheless, some significant differences in neurocognitive functioning between the groups were found. Most of the previous studies on the effects of diabetes on cognitive functioning have found that the critical factors affecting cognitive development in children are early onset of diabetes (Ryan et al. 1985, Rovet et al. 1988, Hagen et al. 1990) and prevalence of severe hypoglycaemia (Rovet et al. 1987, Bjørgaas et al. 1997). However, according to Kaufman and colleagues (1999) age of diagnosis is not related to neurocognitive test results. In our study, the children who had had severe hypoglycaemia were diagnosed at a younger age than the other children with diabetes. This is quite often the case, as young children have a higher incidence of severe hypoglycaemia (Ternand et al. 1982). It remains doubtful, however, whether the onset age of diabetes or the occurrence of severe hypoglycaemia at a certain age affects cognitive development. Because of the small size of the sample, the present study cannot fully differentiate the effects of the age at onset of illness and severe hypoglycaemia.

In children with diabetes, neurocognitive functioning is in most cases normally developed, but diffuse deficits may also exist. Clinically significant impairments are associated with severe hypoglycaemia. Deficits in cognitive functioning in turn have an important effect on the child's performance, on school achievement as well as on the child's ability to manage diabetes. This study suggests that neuropsychological assessments should be administered to children with diabetes in order to identify possible deficits in neurocognitive functioning.

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