Relationship between metabolic control and neurocognitive functions in children diagnosed with type I diabetes mellitus before and after 5 years of age

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SUMMARY: Tolu-Kendir Ö, Kiriş N, Temiz F, Gürbüz F, Önenli-Mungan N, Topaloğlu AK, Yüksel B. Relationship between metabolic control and neurocognitive functions in children diagnosed with type I diabetes mellitus before and after 5 years of age. Turk J Pediatr 2012; 54: 352-361.

We aimed to investigate the effects of age onset of diabetes, glycemic control and frequency of hypoglycemia on neurocognitive functions in type I diabetic children. Sixty type I diabetic children with diagnosis before (Group 1) or after (Group 2) five years of age and 40 healthy children were tested. Wechsler Intelligence Scale for Children Revised (WISC-R), Stroop Test, and Visual Auditory Digit Span Test Form B were applied to all children in the two groups. Neurocognitive functions such as visual perception, short-term memory and selective attention were seen to be negatively affected at a significant level. Group 1 patients with poor glycemic control were found to have significant dysfunction in verbal, performance and general intelligence. Neurocognitive functions were negatively affected by early onset of diagnosis, poor glycemic control and frequent hypoglycemia in children with type I diabetes mellitus. We suggest that negative effects on neurocognitive functions in type I diabetes should be considered in the follow-up of these patients.

Key words: children, type 1 diabetes mellitus, neurocognitive functions, frequency of hypoglycemia.

Diabetes mellitus (DM) is among the most common chronic diseases of childhood and results from a real or functional insulin deficiency. Acute DM complications include diabetic ketoacidosis, brain edema and hypoglycemia; subacute complications include hyperlipidemia and growth retardation, while retinopathy, nephropathy and neuropathy are among chronic complications. One of the less-known and less-mentioned complications of DM is neurocognitive dysfunction[1].

Diagnosis at an early age, frequency of hypoglycemia and poor glycemic control are among the factors negatively affecting neurocognitive functions in type I diabetes mellitus (TIDM)[1].

The pathophysiology underlying this complication is not well understood even though many research findings indicate that both hyperglycemia and hypoglycemia cause neurocognitive dysfunctions in children with TIDM.

The purpose of this study was to investigate the effects of age at onset of diabetes, poor glycemic control and frequency of hypoglycemia on neurocognitive functions in two groups of type I diabetic children aged under five or over five years at diagnosis.

Material and Methods

Patients

The study was performed with 60 type I diabetic patients (6-12 years old) who were followed at the Pediatric Endocrinology Outpatient Department of Çukurova University Medical Faculty. The patients who had abnormal neurologic examination or any other known disease or history of brain injury were excluded from the study. Children with color blindness and uncorrected sensory impairments were

also excluded from the study. The patients were divided into two groups according to the age at diagnosis as those before five years of age (Group 1) or after five years of age (Group 2). Furthermore, the healthy control subjects were recruited from volunteer age-matched children with no known health or learning problems from schools and well-child clinics in the same district. The control group consisted of 40 healthy children (23 females, 17 males) who were age- and gender-matched to the study groups. Socioeconomic status was assessed as "low" or "middle and high" in all groups according to parental education and income. Written informed consent was obtained from parents of all children participating in the research. The study was approved by the institutional ethics committee. The diabetes duration, frequency of symptomatic hypoglycemia, and mean hemoglobin (Hb) A_1c values of all patients were determined. Metabolic control was estimated from HbA1c data in the medical records. Data regarding recent insulin dose were also obtained from the medical records. Patients were asked about the number and time of all previous hypoglycemic events (which required help from another person or hospital admissions) and about the number and time of hypoglycemic comas. Additionally, patients were asked about premature birth and neonatal events, birth weight, brain trauma and diseases of the brain and nervous system, and about other diseases and medication. Occurrence of other diabetic complications was evaluated from the medical records.

B-glucose was measured immediately before and after the cognitive testing. All children were tested in the morning and given breaks and snacks as needed. At the beginning of the assessment session, parents of children with TIDM were asked to check their child's blood glucose prior to the start of the testing. If the child had high (>200 mg/dl) or low (≤70 mg/dl) blood glucose values, blood glucose levels were monitored for providing a euglycemic condition[2]. Cognitive assessment was applied to all children without their being either hypoglycemic or significantly hyperglycemic.

Neuropsychological Assessment

Neurocognitive tests were administered in the same order by an experienced neuropsychologist (NK) who followed a standardized testing protocol. The tester was blind to the clinical status of the participants. The neuropsychological test battery that included four different tests was applied to all groups. These tests are described below.

Wechsler Intelligence Scale for Children–Revised (WISC-R)

The Wechsler Intelligence Scale for Children–Revised (WISC-R)[3] is an index of general intellectual functioning based on the 10 subtests included in the Verbal and Performance (nonverbal) IQ scales. The WISC-R was adapted and standardized in Turkey in 1997. A few items were changed, but in general the Turkish version closely resembles the original version. The standardization sample consisted of 11 age groups between 6–16 years. Reliability was 0.97 and 0.93 for Verbal IQ (VIQ) and Performance IQ (PIQ) scales, while subtest reliability ranged from 0.51 to 0.86[4].

Bender-Gestalt Test (BGT)

First developed by Bender[5], this test is used to evaluate "visual-motor maturity", screen for developmental disorders, or to assess neurological function or brain damage. It measures perceptual motor skills, perceptual motor development, and visual motor integration[6]. Impairment in the listed functions is associated with high scores.

Visual-Aural Digit Span Test-B (VADS-B)

The Visual-Aural Digit Span (VADS-B) test was originally designed as a diagnostic tool for assessing reading and learning disabilities that are mainly functions of the *temporal lobes*; it is specifically used for measuring attention span and multimodal short-term memory function[7,8]. The VADS-B was standardized for Turkish children between the ages of 6–11 years. Test–retest reliability coefficients conducted after a two-month period are between 0.54 and 0.82[9].

Stroop Color Word Interference Test-TBAG Form (SCWT)

The Stroop Color Word Interference Test-TBAG Form (SCWT) is a measure of selective attention and executive functioning. It is most often described as measuring ability to shift cognitive inhibition and ability to

Table I. Demographic and Clinical Characteristics of the Three Groups at the Time of Testing

	Group 1 n=31	Group 2 n=29	Control n=40
Female	n=16 (51.6%)	n=17 (58.6%)	n=23 (57.5%)
Male	n=15 (48.4%)	n=12 (41.4%)	n=17 (42.5%)
Age range at the time of testing	131.3 (72-182)	138.8 (80-190)	125.1 (76-184)
Mean age of diagnosis	44.4	97.2	-
Duration of diabetes	86.9	71.6	-
Mean HbA1c value	8.8	9.5	-
Frequency of hypoglycemia	1.6	1.6	-
Mean age of patients	131.3 (72-182)	138.8 (80-190)	125.1

inhibit an overlearned dominant response in favor of an unusual one (interference)[10-12]. A higher interference score indicates poorer performance[7,8].

Statistical Analysis

The Statistical Package for the Social Sciences (SPSS) 18.0 package program was used in the statistical data analysis. Categorical measurements were summarized as mean and standard deviation (median and minimum–maximum as necessary). The chi-square test was used to compare categorical measures between the groups. The T test was used in independent groups when assumptions were met and the Mann-Whitney U test when assumptions were not met to compare numerical values between groups. In general, one-way ANOVA was used if assumptions were met and the Kruskal-Wallis test when assumptions were not met for the comparison of the numerical values of more than two groups. The Bonferroni, Scheffe or Tamhane tests were used according to the homogeneity of intragroup variances if assumptions were met and the Bonferroni-corrected Mann-Whitney U test if assumptions were not met for the two-way comparison of the subgroups of more than two groups. The statistical significance level was 0.05 in all tests.

Results

There was no statistically significant difference between the patient groups and control group in terms of age and gender. Group 1 included 31 (51.7%) children (onset of diagnosis before 5 years of age) and Group 2 included 29 (48.3%) children (onset of diagnosis after 5 years of age). There were totally 60 children with TIDM in the study groups. The mean age of children in Group 1 was 131.3 months (lower-upper limit: 72-182 months), while the mean age of children in Group 2 was 138.8 months (lower-upper limit: 80-190 months) (Table I). The education levels, socioeconomic levels and residence region of the children's parents in the two patient groups were similar. No statistically significant difference was found between the two patient groups in terms of the number of symptomatic hypoglycemia levels (p: 0.41, Table II).

The mean HbA1c value of the children in Group 1 was 8.77 (min: 5.58, max: 13.4), while in Group 2 it was 9.5 (min: 7.0, max: 13.4).

There was no relation between age onset of diagnosis and IQ scores in children with TIDM. However, the IQ scores of both groups were

Table II. Comparison of Symptomatic Hypoglycemia Frequency between Groups

	Group 1 n (%)	Group 2 n (%)	P
Hypoglycemia frequency	16 51.6	18 62.1	0.41
Less than once per month	15 48.4	11 37.9	
More than once per month	31 100	29 100	
Total			

Table III. Comparison of Neurocognitive Test Scores between Study Groups

	Group 1 (n=31)	Group 2 (n=29)	P
	Mean (min-max)	Mean (min-max)	
WISC-R Verbal score	86.2 (49-117)	86.0 (58-112)	0.97
WISC-R Performance score	86 (50-116)	89.8 (43-128)	0.51
WISC-R Total score	86 (48-114)	87.1 (49-122)	0.87
BGT score	12.4 (4-30)	8 (2-22)	**0.02**
VADS-B Auditory verbal	4.7 (3-7)	5.4 (3-8)	**0.03**
VADS-B Visual verbal	4.5 (3-7)	5.1 (3-7)	0.1
VADS-B Auditory written	4.8 (2-8)	5.5 (4-8)	**0.03**
VADS-B Visual written	4.7 (2-8)	5.6 (3-9)	**0.01**
Stroop B1 period	16.7 (8-70)	13.2 (7-84)	0.39
Stroop B2 period	19.4 (8-100)	10.6 (7-16)	**0.02**
Stroop B3 period	24.3 (9-130)	14.7 (9-31)	**0.002**
Stroop B4 period	32.5 (11-135)	22.8 (11-110)	**0.008**
Stroop B5 period	46.6 (15-142)	29 (16-53)	**0.001**

WISC-R: Wechsler Intelligence Scale for Children-Revised. BGT: Bender-Gestalt test.

VADS-B: Visual-Aural Digit Span Test-B.

in the range of low to normal (Table III).

Comparison of intelligence test scores between the control group and the two study groups revealed that both study groups performed significantly lower than the control group in Information, Arithmetic, Comprehension, Digit Span, Object Assembly, VIQ, PIQ, and Total IQ (Table V).

VADS-B, SCWT and BGT test scores were statistically significantly lower in Group 1 patients than Group 2 patients (Table III).

There was a difference in BGT scores between the study groups. Similarly, there was a difference in BGT scores between the control group and study groups in neurocognitive assessment (Table IV). This finding demonstrated that Group 1 performed significantly lower than Group 2 and the control group in visual motor perception and visual motor integration functions (Table IV).

Intragroup comparison of the neuropsychological test scores in Group 1 according to HbA1c values showed that patients with HbA1c values of ≥8 showed significantly lower performance than patients with HbA1c values <8 in VIQ, PIQ and Total IQ scores (Table VI). On the other hand, patients in Group 2 with HbA1c values of ≥8 scored significantly lower than those with HbA1c values <8 in VIQ and Total IQ scores in the WISC-R and BGT (Table VI).

Comparison of the WISC-R sub-test scores of children in the study groups according to the frequency of symptomatic hypoglycemia revealed that patients in Group 1 with symptomatic hypoglycemia frequency of more than once a month performed significantly lower in the

Table IV. Comparison of Neurocognitive Test Scores between Control Group and the Two Study Groups

	Group 1 n=31 Mean (min-max)	p	Control n=40 Mean (min-max)	P	Group 2 n=29 Mean (min-max)
VADS-B Auditory verbal	4.7 (3-7)	0.35	5 (3-8)	0.7	5.4 (3-8)
VADS-B Visual verbal	4.5 (3-7)	0.10	4.9 (3-7)	0.15	5.1 (3-7)
VADS-B Auditory written	4.8 (2-8)	0.26	5.2 (3-8)	0.86	5.5 (4-8)
VADS-B Visual written	4.7 (2-8)	0.74	5.1 (3-8)	0.2	5.6 (3-9)
ST/B1period	16.7 (8-70)	0.17	14.6 (8-74)	0.38	13.2 (7-84)
ST/B2 period	19.4 (8-100)	1.0	14.8 (7-73)	0.06	10.6 (7-16)
ST/B3 period	24.3 (9-130)	0.46	17.2 (10-35)	0.06	14.7 (9-31)
ST/B4 period	32.5 (11-135)	1.0	27.3 (12-63)	0.06	24.8 (11-110)
ST/B5 period	46.6 (15-142)	0.34	37 (20-111)	0.068	29 (16-53)
BGT score	12.4 (4-30)	0.0001	6.9 (1-16)	0.96	8 (2-22)

VADS-B: Visual-Aural Digit Span Test-B. ST: Stroop test. BGT: Bender-Gestalt test.

VIQ subtests and Block Design subtest of PIQ than patients with a frequency of less than once a month. On the other hand, the effect of symptomatic hypoglycemia frequency on WISC-R scores was not statistically significant in Group 2 (Table VII).

Comparison of Stroop test periods of the two study groups with respect to frequency of hypoglycemia showed that Group 2 patients with a frequency of hypoglycemia of more than once a month had a significantly (p: 0.04) longer test period in the 5th part of the Stroop test than patients with a frequency of less than once a month (p>0.05;Table V).

Discussion

In this study, we found that neurocognitive functions were negatively affected in children with DM diagnosed at an early age. In contrast, no significant difference was found between the patient groups in terms of WISC-R scores when the IQ scores of the patients were analyzed. The closer metabolic control of early diagnosed patients may play a role in this finding. Northam et al.[23] similarly found no significant difference between children with TIDM diagnosed under four and over four years of age in terms of VIQ, PIQ and Total IQ mean scores. However, some studies have indicated that the age at diagnosis negatively affects IQ scores[14,15].

Children with early diagnosis of TIDM had lower scores for visual spatial abilities and short-term memory on the VADS-B and BGT tests in our study.

Gaudieri et al.[16,17] reported that visual and auditory short-term memory and attention as well as cognitive functions such as learning ability are affected more profoundly in early-onset diabetes. Previous studies conducted in children under five years of age at diagnosis have also reported that DM mostly affects the acquisition of visual spatial skills negatively[18]. Rovet and Alvarez[14] found a significant deterioration in the attention, concentration and memory functions of children diagnosed with TIDM under six years of age, similar to our study.

We found that diagnosis of TIDM at an early age had a negative effect on Stroop test performance. This finding indicates that frontal lobe functions such as selective attention,

Table V. Comparison of Intelligence Test Scores between Control Group and the Two Study Groups

	Group 1 n=31	p	Control n=40	p	Group 2 n=29
	Mean (min-max)		Mean (min-max)		Mean (min-max)
Information	6.4 (1-15)	0	9.5 (6-15)	0	6.8 (1-13)
Similarities	9.4 (1-15)	0.1	9.9 (5-13)	1	9.6 (3-14)
Arithmetic	7.9 (1-14)	0	10.5 (7-14)	0	7.7 (2-15)
Comprehension	9 (3-29)	0.02	9.5 (7-13)	0.01	8 (4-12)
Digit span	7.5 (2-17)	0.02	8.8 (5-12)	0.01	7.7 (3-15)
Picture completion	8.2 (1-18)	0.5	10.5 (3-17)	0.2	7.4 (1-14)
Picture arrangement	7.4 (1-14)	0.1	9 (4-18)	0.5	7.2 (1-12)
Block design	9.2 (3-17)	0.1	10.5 (7-15)	0.2	9.2 (3-17
Object assembly	8.5 (3-17)	0	11 (6-19)	0	8.9 (2-19)
Coding	9 (3-15)	0.1	9.9 (7-15)	0.2	10.9 (2-18)
VIQ	86.2 (49-117)	0	96.8 (70-112)	0	86 (58-112)
PIQ	88.7 (50-116)	0.04	98.6 84-112	0.03	89.8 43-128
TIQ	86.2 (49-117)	0.01	98.6 (83-112)	0.01	98.9 (70-112)

VIQ: Verbal IQ. PIQ: Performance IQ. TIQ: Total IQ.

information-processing speed and response inhibition task are more prone to deteriorate in children diagnosed with TIDM in early childhood. Rovet and Alvarez[14] supported our results in their study on adolescents using the Stroop test by reporting that patients diagnosed at an early age are more prone to be influenced by the disruptive effects of distractors and as a result are unable to control automatic responses compared to patients diagnosed at a late age and healthy controls.

Children with TIDM diagnosis under the age of five had low scores in the VIQ, PIQ and Total IQ. Similarly, children with TIDM diagnosis over the age of five had low scores in the VIQ and Total IQ. These findings of our study suggest that poor metabolic control negatively affects IQ scores regardless of the age at diagnosis. Perantie et al.[19] similarly reported that high HbA1c levels are associated with low VIQ scores in children with TIDM. Musen and colleagues[20] reported a relationship between high HbA1c levels and low Total IQ and PIQ scores. Poor metabolic control was also found to negatively affect the BGT performance of children diagnosed over the age of five. Similar to our results, psychomotor development and memory functions were found to be worse in those with poor glycemic control in two separate studies of Perantie[19] and Musen[20]. Fine motor control was also reported to be affected more profoundly in children with TIDM with a high HbAc1 value in a prospective study carried out by Hershey et al.[21,22]

It is noteworthy that we observed poor performance in only the visual written subtest of the VADS-B in children diagnosed over the age of five with poor glycemic control. Visual attention, visual memory and auditory attention, auditory memory functions are

Table VI. Comparison of Neurocognitive Test Scores of Groups According to HbA1c Levels

	Group 1 (n=31) HbA1c		p	Group 2 (n=29) HbA1c		p
	≤8 Mean (min-max) n=15	>8 Mean (min -max) n=16		≤8 Mean (min-max) n=13	>8 Mean (min-max) n=19	
WISC-R Verbal score	95.7 (80-114)	80.9 (49-117)	0.03	100.7 (87-112)	80.5 (58-111)	0.003
WISC-R Performance score	104 (91-116)	81.4 (50-107)	0.0001	100.1 (86-128)	86 (43-120)	0.10
WISC-R Total score	99.9 (86-106)	79.5 (48-114)	0.001	100.3 (86-122)	82 (49-108)	0.018
VADS-B Auditory verbal	4.5 (3-7)	4.8 (3-7)	0.44	5.3 (3-7)	5.4 (4-8)	0.68
VADS-B Visual verbal	4.5 (3-6)	4.5 (3-7)	0.98	5.5 (4-7)	4.9 (3-7)	0.23
VADS-B Auditory written	4.5 (3-6)	4.9 (2-8)	0.44	6 (5-8)	5.3 (4-7)	0.15
VADS-B Visual written	4.5 (2-8)	4.8 (2-7)	0.46	6.5 (5-9)	5.3 (3-7)	0.05
Stroop test B1 period	12.3 (9-19)	18.8 (8-70)	0.95	10.75 (7-16)	14.2 (7-84)	0.95
Stroop test B2 period	13.3 (10-24)	22.4 (8-100)	0.76	10.5 (7-13)	10.3 (7-16)	0.75
Stroop test B3 period	21.5 (13-37)	25.6 (9-130)	0.57	12.8 (9-17)	15.5 (9-31)	0.57
Stroop test B4 period	32.1 (19-57)	32.7 (11-135)	0.49	16.5 (11-25)	25.3 (12-110)	0.49
Stroop test B5 period	50.1 (31-142)	45 (15-136)	0.79	23.1 (16-37)	31.3 (17-53)	0.79
BGT score	11 (4-21)	13.1 (5-30)	0.41	6.1 (3-10)	8.8 (2-22)	0.075

WISC-R: Wechsler Intelligence Scale for Children-Revised. VADS-B: Visual-Aural Digit Span Test-B.

BGT: Bender-Gestalt test.

thought to be more prone to deteriorate in the presence of poor glycemic control.

The high frequency of hypoglycemia in children diagnosed at an early age has been found to negatively affect especially the PIQ and Total IQ. There may be two reasons for this finding. The first is the developing central nervous system and especially myelinization being affected by the hormonal and physical changes in this critical period; the second is the difficulty of establishing metabolic control in children at a very young age in the early development period. Northam et al.[23] studied 116 children with TIDM with ages ranging from 3 to 14 and reported that children diagnosed under the age of five had a lower Total IQ score as measured with WISC-R. Similar results were reported in two previous studies by Rovet[24,25]. Ryan and colleagues[26] revealed that this difference is especially prominent under the age of five.

The negative effect on only the patterns with block design test in the WISC-R in children diagnosed under the age of five with a high frequency of hypoglycemia and the consistency with the BGT result indicate that children diagnosed with DM at an early age have a visual perception dysfunction.

The lack of a significant effect of the frequency of hypoglycemia on the VADS-B and BGT test results in our study may arise from the small number of patients in the groups and the use of different tests in other studies. A high frequency of hypoglycemia was found to have a negative impact on SCWT performance in children diagnosed over five years of age in our

Table VII. Comparison of Neurocognitive Test Scores of Study Groups According to Frequency of Hypoglycemia

	Group 1 (n=31) Hypoglycemia			p	Group 2 (n=29) Hypoglycemia			p
	Less than once per month	More than once per month	Total		Less than once per month	More than once per month	Total	
	Mean (min-max)	Mean (min-max)	Mean (min-max)		Mean (min-max)	Mean (min-max)	Mean (min-max)	
WISC-R Verbal score	89.4 (49-117)	81.7 (52-106)	85.7 (49-117)	0.20	89.2 (64-112)	80.9 (58-111)	86.1 (58-112)	0.20
WISC-R Performance score	96.3 (61-116)	80.5 (50-105)	88.7 (50-116)	0.01	93.2 (66-128)	84.3 (43-113)	89.8 (43-128)	0.41
WISC-R Total score	92.3	79.4 (48-100)	86.0 (48-114)	0.01	90.2 (64-122)	82.0 (49-112)	87.1 (49-122)	0.36
Picture completion	9.5 (5-18)	6.9 (1-11)	8.2 (1-18)	0.09	8.3 (3-14)	5.9 (1-11)	7.4 (1-14)	0.15
Picture arrangement	8.0 (1-12)	6.3 (1-14)	7.2 (1-14)	0.12	7.7 (1-12)	6.6 (1-11)	7.3 (1-12)	0.46
Block design	10.5 (7-17)	7.8 (3-17)	7.2 (3-17)	0.01	9.5 (3-17)	8.0 (3-14)	8.9 (3-17)	0.36
Coding	10.3 (5-15)	7.9 (3-14)	9.1 (3-15)	0.06	11.2 (4-17)	10.6 (2-18)	11.0 (2-18)	0.80
Object Assembly	9.0 (5-12)	7.9 (3-17)	8.5 (3-17)	0.14	9.6 (5-19)	7.6 (2-12)	8.8 (2-19)	0.23
Stroop test B1 period	11.2 (8-19)	22.6 (8-70)	16.7 (8-70)	0.15	14.3 (7-84)	11.4 (8-14)	13.2 (7-84)	0.14
Stroop test B2 period	12.5 (8-24)	26.8 (8-100)	19.4 (8-100)	0.29	10.1 (7-13)	11.6 (8-16)	10.6 (7-16)	0.13
Stroop test B3 period	19.9 (10-37)	29.0 (9-130)	23.4 (9-130)	0.98	14.0 (9-27)	15.9 (12-31)	14.7 (9-31)	0.18
Stroop test B4 period	30.0 (13-57)	32.2 (11-135)	32.5 (11-135)	0.74	19.0 (11-36)	29.1 (16-110)	22.8 (11-110)	0.08
Stroop test B5 period	46.1 (20-142)	47.2 (15-136)	46.6 (15-142)	0.74	25.5 (16-53)	33.2 (18-49)	29.0 (16-53)	0.04

VADS-B Auditory verbal	4.6 (3-7)	4.8 (3-7)	4.7 (3-7)	0.68	5.3 (4-7)	5.5 (3-8)	5.4 (3-8)	0.67
VADS-B Visual verbal	4.4 (3-6)	4.6 (3-7)	4.5 (3-7)	0.74	5.3 (4-8)	4.8 (3-7)	5.10 (3-7)	0.32
VADS-B Auditory written	4.8 (3-7)	4.8 (2-8)	4.8 (2-8)	0.89	5.5 (4-9)	5.5 (5-7)	5.5 (4-8)	0.81
VADS-B Visual written	4.6 (2-8)	4.9 (2-7)	4.7 (2-8)	0.47	5.8 (4-9)	5.5 (3-7)	5.7 (3-9)	0.74
Bender Gestalt Test	11.9 (4-21)	13 (5-30)	12.5 (4-30)	0.95	7.1 (3-11)	9.6 (2-21)	8.1 (2-21)	0.36

WISC-R: Wechsler Intelligence Scale for Children-Revised. VADS-B: Visual-Aural Digit Span Test-B.

study. Brands et al.[27] and Ryan[28] emphasized that exposure to severe hypoglycemia delays the speed of information processing in their study on children with TIDM where the Stroop test was used in different age groups. Finding the SCWT performance low only in the group diagnosed over the age of five may depend on a lower percentage following the diet and consequently having a higher frequency of hypoglycemia, as the average age of the group was in the adolescence period.

In conclusion, neurocognitive functions including visual motor development, visual spatial memory, visual organization, visual perception, multimodal short-term memory, concentration, selective attention, and speed of information processing were found to be negatively affected in children diagnosed with TIDM at an early age. VIQ, PIQ and Total IQ were also found to be significantly impaired in children diagnosed with TIDM at an earlier age along with poor glycemic control. On the other hand, poor metabolic control by itself was determined to negatively affect visual motor functions, visual perception, visual attention, visual spatial memory, and visual organization skills. In addition, selective attention and speed of information processing were impaired in children with a high frequency of hypoglycemia independent of the age at diagnosis.

REFERENCES

1. Christopher TK, Elizabeth R. Cognitive dysfunction and diabetes mellitus. Endocr Rev 2008; 29: 494-511.
2. American Diabetes Association. Standards of medical care in diabetes. Diabetes Care 2007; 30: 4–41.
3. Wechsler D. Manual for the Wechsler Intelligence Scale for Children–Revised. New York: Psychological Corporation; 1974.
4. Savaşır I, Şahin N. Wechsler Çocuklar İçin Zeka Ölçeği (WISC-R). Ankara: Türk Psikologlar Derneği; 1997.
5. Bender L. A Visual-Motor Gestalt Test and Its Clinical Use. New York: American Orthopsychiatric Association; 1938: 3.
6. Lezak MD. Neuropsychological Assessment. New York: Oxford University Press; 1995: 234.
7. Karakas S, Yalın A. GISD-B Kullanlm Kılavuzu. Ankara: Eryılmaz Ofset; 2009.
8. Koppitz EM. The Visual Digit Span Test. New York: Grune and Stratton; 1977.
9. Karakaş S, Yalın A. Görsel İşitsel Sayı Dizileri Testi-B Formu. Ankara: Medikomat; 1993.
10. Stroop JR. Studies of interference in serial verbal reactions. J Exp Psychol 1985; 18: 643-662.

11. Golden CS. Stroop Color and Word Test: A Manual for Clinical and Experimental Uses. Chicago: Stroelting Go; 1978.
12. MacLeod CM. The Stroop task: the "gold standard" of attentional measures. J Exp Psychol Gen 1992; 121: 12-14.
13. Ryan C, Becker D. Hypoglycemia in children with type 1 diabetes mellitus: risk factors, cognitive function, and management. Endocrinol Metab Clin North Am 1999; 28: 883–900.
14. Rovet J, Alvarez M. Attentional functioning in children and adolescents with type 1 diabetes. Diabetes Care 1997; 20: 803-810.
15. Holmes CS. Neuropsychological profiles in men with insulin dependent diabetes. J Consult Clin Psychol 1986; 54: 386–389.
16. Gaudieri PA, Chen R, Greer TF, Holmes CS. Cognitive function in children with type 1 diabetes–a meta-analysis. Diabetes Care 2008; 31: 1892–1897.
17. Perantie DC, Lim A, Wu J, et al. Severe hypoglycemia vs. hyperglycemia: unique effects on cognition in youth with type 1diabetes mellitus (TIDM). Diabetes 2007; 56: 1887.
18. Priscilla A, John EO. The neurocognitive effects of type 1 diabetes mellitus in children and young adults with and without hypoglycemia. J Dev Phys Disabil 2009; 21: 425–440.
19. Perantie DC, Lim A, Wu J, et al. Effects of prior hypoglycemia and hyperglycemia on cognition in children with type 1 diabetes mellitus. Pediatr Diabetes 2008; 9: 87-95.
20. Musen G, Jacobson AM, Ryan CM, et al. Impact of diabetes and its treatment on cognitive function among adolescents who participated in the diabetes control and complications trial. Diabetes Care 2008; 31: 1933-1938.
21. Hershey T, Lillie R, Sadler M, White NH. A prospective study of severe hypoglycemia and long-term spatial memory in children with type 1 diabetes. Pediatr Diabetes 2004; 5: 63–71.
22. Hannonen R, Tupola S, Ahonen T, Riikonen R. Neurocognitive functioning in children with type-1 diabetes with or without episodes of severe hypoglycaemia. Dev Med Child Neurol 2003; 45: 262–268.
23. 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.
24. Rovet JF, Enhrlich RM, Hoppe M. Specific intellectual deficits in children with early onset diabetes mellitus. Child Dev 1988; 59: 226–234.
25. Rovet JF, Ehrlich RM, Czuchta D. Intellectual characteristics of diabetic children at diagnosis and one year later. J Pediatr Psychol 1990; 15: 775-788.
26. Ryan C, Longstreet C, Marrow L. The effects of diabetes mellitus on the school attendance and school achievement of adolescents. Child Care Health Dev 1985; 11: 229-240.
27. Brands A, Biessels GJ, de Haan EH, Kappelle LJ, Kessels RP. The effects of type 1 diabetes on cognitive performance. Diabetes Care 2005; 28: 726-735.
28. Ryan C. Does moderately severe hypoglycaemia cause cognitive dysfunction in children? Pediatr Diabetes 2004; 5: 59-62.