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Effect of Type I Diabetes on Cognitive Functions of School-Age Children

Okul Çağındaki Çocuklarda Tip I Diyabetes Mellitusun Bilişsel Fonksiyonları Üzerine Etkisi

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Abstract

Aim: Carbohydrates have important effects on the development and function of the nervous system. We propose to determine the effect of type I diabetes on cognitive functions of school-age children.

Materials and Methods: The research was conducted on 29 children with type I diabetes mellitus. Subjects were chosen from amongst the patients who were admitted to the pediatric endocrinology department of Turgut Özal Health Center (Malatya, Turkey). In addition, 28 children without any apparent health problems were chosen as controls.

Subjects were divided into four groups according to their age; two of these groups included children with diabetes and the other two the controls. Wechsler intelligence test, which was developed for children, was applied to control and patient groups by pediatric psychologists.

Results: We identified that type I diabetes influenced the abilities of visual-spatial groups in different ways. We observed that it was influential on visual-hearing remembrance and ability to employ acquired knowledge of various age groups of children with numerous intelligence types. In general, we noticed statistically significant differences in word sequencing, picture completion and designing the picture abilities between the groups. A positive correlation was identified between the cubical figure and performance scores of the two diabetic children groups.

Discussion: We reviewed the results in the light of the relevant literature. Diabetes was found to affect specific type of memory inversely. Therefore, it can be concluded that time of diagnosis and ensuring metabolic control in diabetes might have important consequences associated with the hazardous effects of diabetes on the development and function of the nervous system.

Keywords: Diabetes Mellitus (Type I); Cognitive Function; Schoolchildren; Wechsler Intelligence Scale For Children–Revised.

Öz

Amaç: Sinir sisteminin gelişimi ve fonksiyonları bağlamında karbonhidratlar büyük bir öneme sahiptir. Bu nedenle; okul çağındaki çocuklarda, karbonhidrat metabolizmasının bozulduğu tip I diyabet mellitus'un bilinçsel fonksiyonları üzerindeki etkisini saptamayı amaçladık.

Gereç ve Yöntem: İnönü Üniversitesi Tıp Fakültesi Araştırma ve Uygulama Merkezi Çocuk Endokrinoloji polikliniğine başvuran, tip I diyabet mellitus tanısı konulan 6-16 yaş aralığında diyabet dışında başka bir hastalığı olmayan 29 çocuk ve akranlarından seçilen 28 sağlıklı çoçuk, yaş aralıklarına göre dört gruba ayrıldı. Çalışmaya katılanlar iki diyabet ve iki kontrol grubu şeklinde ayrıldı. Hasta ve kontrol grubundaki çocuklara çocuk psikiyatrisine bağlı olarak çalışan uzmanlar tarafından ve çocuklar için geliştirilen Wechsler çocuklar için zeka testi uygulandı.

Bulgular: Tip I diyabetin, farklı yaş gruplarındaki çocuklar arasında görsel- mekansal yetenek ve görsel- işitsel uyaranların sırasını hatırlama ve kazanılan bilginin sorunları çözmede kullanma yeteneği bakımından zekanın değişik biçimlerini farklı düzeyde etkilediği saptandı. Gruplar arasında genel çerçevede söz dizisi, resim tamamlama ve resim düzenleme bakımından istatistiksel olarak farklılar saptandı. Her iki diyabet grubunda çocukların küplerle desen puanı ve performans puanı arasında pozitif bir korelasyon saptandı.

Sonuç: Bulgular literatüre göre tartışıldı. Çocuklarda; tip I diyabetin, belli zeka tipleri üzerinde olumsuz etki yaptığı saptandı. Bu nedenle erken tanı ve metabolik kontrolün sağlanması diabetin olası zararlı etkilerinin önlenmesi bakımından önemli olduğu düşünülmektedir.

Anahtar Kelimer: Tip I Diyabet; Bilişsel Fonksiyonlar; Okul Çağındaki Çocuklar; Wechsler Zeka Testi (Çocuklar İçin).

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INTRODUCTION

Type I Diabetes Mellitus is a widespread metabolic disease which is seen during the childhood and adolescents. This disease is characterized by the high level of carbohydrate in plasma and appears in the absolute deficiency of the synthesize and secretion of insulin via damaged of the beta cell of in the islets of Langerhans via autoimmune (1-3)

The Type I Diabetes is a disease that affects many organs in the body as a result of deterioration of carbohydrate metabolism and deterioration of fat and protein metabolism (4). The nervous system is one of the target organs of this disease (5). The provision of uninterrupted glucose for the normal functions of the nervous system has a critical importance, which is especially important for children. In children, glucose is necessary for brain growth and development. For this reason, the children's brain is more susceptible to the changes that occur in this period (6). Diabetes causes acute effects such as diabetic ketoacidosis, brain edema, and hypoglycemia on one side, and many chronic changes including retinopathy, nephropathy, and neuropathy on the other side (2,5,7).

Glucose is the brain's primary energy source. Normally, glucose's continuous supply by blood flow is required. Diffusion facilitated by glucose transport proteins is provided by the micro-vessel endothelial cells of the brain (8). Hyper- and hypoglycemia in childhood and adolescence causes adverse effects on the development of the nervous system cells on the one side, while the relationship between Type I Diabetes mellitus and some neurodegenerative diseases leads to the increasing importance of early diagnosis(9).

The effects on the diabetic nervous system were studied by various radiological methods which include the encephalogram, changes in the amount of gray and white matter intensities, and the effect of the thickness of the cerebral cortex layer(10).

Diabetic hyper- and hypoglycaemic changes caused by vascular changes in children and damage to neuronal cells cause children to fall behind in their growth and development of the brain relative to their peers, thereby causing them to back up at school and in life(3). This is why early identification of diabetes in children and the initiation of the necessary treatment are important for Type I diabetes causing a more limited injury.Comparisons were made with healthy children in the context of determining the effect of cognitive functions of Type I diabetes on those whose disease began at an early age in later childhood and adolescence. Type I Diabetes has been reported to lead to impaired intelligence, school success, visual-spatial ability, memory, attention and executive functions, rapid decision making, problem solving skills, learning, writing, reading, attention and psychological efficacy in children (2, 11). Assessments made with non-diabetic children with magnetic resonance imaging have been reported to result in an increase in cortical atrophy and more brain stem lesions, mainly in subcortical areas, slowing of brain stem evoked potential transmission, and abnormalities in most regional blood flow perfusion (11).

With neuropsychological tests, a number of studies have been conducted to determine the effects of changes in Type I diabetes in different regions of the brain, and to assess the effects of different regions on their daily life. Each of these tests is different from each other in both the context of the goal and the functions performed by the different regions of the brain. Relationship with memory and intelligence is the most studied basic mental abilities (12). But, the results of studies on this subject are contradictory. With this conflicting data in mind, we aimed to use Wechsler's identify the intelligence scale reviewed form for children and to identify the level and level of mental levels of children with Type I diabetes according to their peers and to explain the possible mechanism.

Identification of diabetes in children and changes in lifestyle with high metabolic control strength and high calorie diet are leading to an increase in the prevalence of diabetes in the community. Our aim is to demonstrate the effect of diabetes on neurocognitive functions by early diagnosis and metabolic control and to determine the level of mental status of diabetic children relative to their peers.

MATERIALS and METHODS

This study was carried out in 29 patients with Type I diabetes, who had no other known disease, no central trauma and normal neurological examination followed in the pediatric endocrinology clinic of Inonu University. The control group consisted of 28 healthy children. The patients and the control group were divided two groups according to an interval of their age (6-11 and 12-16).

Gender, age, the area of residence, mother-father age, education and occupations, socioeconomic status of their families, living areas were recorded in the diabetic groups studied.

Healthy children and children with diabetes were taken into the study group were composed of a first group of 6 to 11 of years old and the second group of 12 to 16-year-olds. Among diabetic children, the first group children consisted of aged 12-16 years and the second group consisted of aged 6-11 years. Among the children in the control group, those in the 6-11 age group constituted the third study group, while those in the 12-16 range constituted the fourth study group. Every child participating in the study and their parent/guardian were given detailed information about the pre-accession work, and the informed consent was obtained. The study was approved by the Ethics Committee of Inonu University Medical Faculty.

In the evaluation of cognitive functions, Wechsler's intelligence scale-revised form for children (WISC-R) was used. The test was applied by a specialist psychologist working at Inonu University Children's Psychiatry Department. Wechsler's Intelligence Scale Form revised for children was used to identify children's intelligence levels and identify problems they are experiencing

2016;23(1):36-41
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(Wechsler Intelligence Scale for Children Revised –WISC-R). This scale, developed by Wechsler in 1949, was revised in 1974 and emerged in the form of WISC - R (Revised) (12).

WISC-R scale consists of two parts; verbal and performance. In the calculations, three types of scores are calculated: verbal, performance, and full scale. Each of these sections consists of six sub-tests and a total of twelve sub-tests. Verbal section consists of information, Similarities, Arithmetic, Vocabulary, Comprehension and Digit span. Performance section consist of picture Completion, picture arrangement, block design, Object Assembly, Coding and Mazes subtests.

In WISC-R, the individual's score is from a sub-test is the sum of the scores given to the items in that sub-test. The raw scores obtained are converted into standardized score which prepared them according to age and monthly slices of the calendar year of the child. The sum of the standard scores obtained for the verbal subtests yields the Performance Intelligence Division (PID), the sum of the standard scores obtained for performance subsets yields Verbal Intelligence Department score (VID) of the individual. In this study, the numerical order of the subtest scores were not used in the calculation of the verbal sub-test, verbal IQ, and full intelligence scores. In a similar manner, while calculating the performance intelligence and total intelligence scores, the scores of subtest of the maze were not included. The total intelligence score was calculated from the collection of verbal and performance scores.

WISC-R; standardization in our country was carried out by Savaşır et al.in 1995, on a sample of 1639 persons whose are between 6-16 years old (12). In the reliability study of WISC-R on Turkish children, the semi-reliability of the tests was 0.97 for the verbal section, 0.93 for performance section, and 0.97 for the total section. These values show that WISC - R has high reliability (13).

In the WISC - R; one of the verbal sub-tests and all of the performance tests are time limited. The test can be applied by the specially trained personnel. This scale developed by Wechsler can be used to see the place of the child's according to in his or her own age, to evaluate the verbal and visual memory separately, and looks to at both memory and learning not only instant memory but also the delayed memory. As a result of the evaluation, coefficients of the verbal, performance and all test intelligence parts of the individuals are obtained. According to the rules of the test, if the verbal intelligence section score is 15 points lower than the score of the performance intelligence section it may be considered that there is a problem in the language area. On the other hand, if the performance intelligence section score is 15 points lower than the verbal intelligence section, it may be considered that the problem in the visual-motor - perceptual area.

The intelligence score obtained as a result of the intelligence test is called IQ. In this classification, 130 and above; very intelligent, between 120 and 129; superior, between 110 and 119; average / brighter, between 90 and 109; average / normal intelligence, between 80-90 points; blunt, between 70-79 points; limited mental functioning, between 69 and below points; mentally disabled(13).

SPSS version 13.00 was used for statistical evaluation. The mean standard deviation (SD) and median (min-max) were used for the quantitative variables and the numeric and percentage for the qualitative variables. The normal distribution of the data on quantitative variables was assessed by the Shapiro Wilk normality test. One-way analysis of variance and the least significant difference method were used in the comparison of the quantitative variables with normal distribution. Kruskal- Wallis variance analysis and Benferonian Mann-Whitney U test were used for those with abnormal distribution. In the evaluation of qualitative variables was assessed by Pearson Chi-square, Spearman Rank correlation analysis, and Fisher's exact Chi-square analysis. P value≤0.05 were considered statistically significant.

RESULTS

This study was done with the 28 healthy children and 29 Type I diabetes children who followed for a period of two years. The patient and control group age range was between 72-192 months. Patients group were divided into two groups according to their age range. 12-16 age group (1st group) and 6-11 years old group (2nd group) was assembled. Fifteen children (51.7%) were in the first group and 14 (48.3%) were in the second group.

The average age of the children in group 1 was 131.3 months (lower-upper limit: 144-192 months), while the average age of the children in the second group was 118.8 months (upper and lower limit: 72-132 months). The difference between the ages of the children in the first and second groups was statistically significant (p <0.0001).

The third group of the study age were between 6-11 years and constitute the first control group (72-132 months), while the fourth group of the study were between 12 and 16 years of age (144-192 months) there was no statistically significant difference in the between the control groups according to the age range. The mean age between the third study group (first control group) and the second study group (second patient group) was statistically significant. (p<0.0001).

Mean age of diagnosis of the patients in our study was 44.4 months (min: 12 month- max: 63 months) in the first group, whereas 97.2 months (min: 63 months, max: 149 months) in the second group. The mean duration of disease was 86.9 months (min: 33 months, max: 24 months) in the first group and 71.5 months (min: 28 months, max: 132 months) in the second group.
When the evaluating the scores of verbal subtests, there was a statistical difference between the groups in terms of picture completion and picture arrangement in comparison between the groups (Table-1)

2016;23(1):36-41
DOI:10.5455/jtomc.2015.10.024

Table 1. Comparison of the study and control groups in the age range of 6-16 years a score in terms of İnformation, arithmetic, vocabulary, picture completion and picture arrangement score.

	Grup I (mean±SD)	Grup İİ (mean±SD)	Grup İİİ (mean ±SD)	Grup İV (mean±SD)	P
İnformation	7.07±2.3	7.26±3.7	8.64±2.7	9.35±3.1	0.153
Arithmetic	9.42±2.9	9.13±3.1	10.92±2.7	10.92±2.4	0.185
Vocabulary	8.28±1.8	8.06±1.6	9.64±1.5	8.28±1.4	0.056
Picture completion	8.21±3.4	9.26±2.9	11.07±1.8	10.07±2.3	0.050
Picture arrangement	8.35±2.4	7.86±2.5	11.71±3.3	7.50±3.9	0.03

There was a statistically significant difference between the groups in terms of picture arrangement, vocabulary and picture completion.

Table 2. Comparison of study and control groups in the age range of 6-16 years in terms of similarity, vocabulary, comprehension, block design, the piece combining and the coding scores

	Grup İ (mean2, min-max)	Grup II (mean2,min-max)	Grup İİİ (mean2, min-max)	Grup İV4 (mean2,min-max)	P
Similarity	10.00(9-16)	9.00(6-15)	12.00(7-15)	10.00(4-14)	0.105
Vocabulary	8.00(7-16)	8.00(1-13)	11.00(8-14)	9.00(6-12)	0.153
Comprehension	10.00(5-13)	11.00(5-15)	11.00(8-14)	11.50(7-12)	0.490
Block design	9.00(3-17)	10.00(4-15)	10.00(7-15)	10.00(5-15)	0.182
Piece combining	9.50(7-17)	10.00(6-14)	10.00(7-13)	9.50(6-14)	0.823
Coding	8.50(6-14)	10.00 (7-34)	10.00(7-15)	9.00 (5-17)	0.275

There was no statistical difference between groups in the context of quantitative data without normal distribution.

There was a positive correlation between the score of block design and performance score among the diabetic groups(group I r=0.657,p=0.011, Group II r=0.836,p=0.0001)

Table 3. Comparison of the study and control groups in the age group of 6-11 with respect to İnformation, arithmetic, vocabulary, picture completion and picture arrangement scores

	Grup İİ (mean,±,SD)	Grup İİİ (mean,±,SD)	p
Information	7.26±3.7	8.64±2.7	0.273
Arithmetic	9.13±3.1	10.92±2.7	0.110
Vocabulary	8.06±1.6	9.64±1.5	0.014
Picture completion	9.26±2.9	11.07±1.8	0.063
Picture arrangement	7.86±2.5	11.71±3.3	0.002

A statistically significant difference was found between the groups in terms of picture arrangement and vocabulary

Table 4. Comparison of study and control groups in the age range of 12-16 years in terms of ınformation, arithmetic, Vocabulary, picture completion and picture arrangement scores.

	Grup İ (mean,±,SD)	Grup İV (mean,±,SD)	P
Information	7.07±2.3	9.35±3.1	0.039*
Arithmetic	9.42±2.9	10.92±2.4	0.152
Vocabulary	8.28±1.8	8.28±1.4	1.000
Picture completion	8.21±3.4	10.07±2.3	0.107
Picture arrangement	8.35±2.4	7.50±3.9	0.503

There was a statistically significant difference between the two groups in terms of information subtest, but not in other items.

Table 5. Comparison of study and control groups in the 6-11 age range in terms of similarities, vocabulary, comprehension, block design, piece combining, coding, verbal and full scores.

	Grup İİ (mean2- min-max)	Grup İİİ (mean2-min-max)	P
Similarities	9.00 (9-15)	12.00(7-15)	0.036
Vocabulary	8.00(1-13)	11.00(8-14)	0.037
Comprehension	11.00(5-15)	11.00(8-14)	0.675
Block design	10.00(4-15)	10.00(7-15)	0.322
Piece combining	10.00(6-14)	10.00(7-13)	0.424
Coding	10.00(7-34)	10.00(7-15)	0.575
Verbal score	95.00 (58-120)	101.00(90-128)	0.080
Fullscore	97.00 (63-121)	104.00(93-128)	0.038

Although there was a statistical difference between the second and third groups in terms of similarities, vocabulary and full scores, no difference was found in terms of other variables.

2016;23(1):36-41
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Table 6. Comparison of study and control groups between 12-16 years of age in terms of similarities, vocabulary, comprehension, block design, the piece combining, coding, verbal and full scores.

	Grup İ (mean2, min-max)	Grup İV (mean2, min-max)	P
Similarities	10.00(9-16)	10.00(4-14)	0.376
Vocabulary	8.00(7-16)	9.00(6-12)	0.671
Comprehension	10.50(5-13)	11.50(7-12)	0.420
Block design	9.00(3-17)	10.00(5-15)	0.044
Piece combining	9.50(7-17)	9.50(6-14)	0.907
Coding	8.50(6-14)	9.00 (5-17)	0.658
Verbal score	90.50(81-126)	97.00(70-117)	0.333
Full score	91.00(79-119)	95.00(73-123)	0.240

There was only a difference between the first and fourth groups in terms of the context of the block design. There was no significant difference between the groups in terms of other data examined.

DISCUSSION

Because the effect of diabetes on neurocognitive functions depends on the disease process and on the age of onset of the disease, children were divided into two groups based on the age ranges of 6-11 and 12-16 years. In this study, we evaluated the neurocognitive functions of children with diabetes mellitus and healthy children with age above 6 years and 16 years. In the evaluation of neurocognitive functions, the relationship between WISC-R intelligence scale and intelligence-age and neurocognitive functions were examined. Normally, for the normal neuronal function of the central nervous system, the glucose content is dependent on the continuous blood flow and supply of the glucose importance vital. Abnormal blood glucose concentration can cause temporary or permanent changes in the central nervous system. This is especially important for children since during the first years of life in children, glucose energy requirement increase for the brain to grow and develop. Exposure to the hyperglycemia for a long time can lead to neuronal damage with many mechanisms (8,14-16). The brain is metabolically very active and consumes energy disproportionately to with its size. In adults, although brain weight does represent 2% of body weight, however, oxygen consumption accounts for 20% of the oxygen consumed by the body and takes 15% of the heart output. At childhood (5-6 years of age), brain oxygen consumption at rest is approximately 50% of total body oxygen consumption(14). Diabetes mellitus is largely related to mild dysfunction of the brain(11,14-15). Between the first 4-7 years of life, the development of diabetes greatly increases the risk of impairment in cognitive function (16). A wide variety of neuropsychological tests related to the purpose of detecting intelligence are used to demonstrate the magnitude of the damage caused by diabetes in the central nervous system. Intelligence is a general natural ability to person realize the functions that are related to different cerebral zones, which enable the person to cope with the perception of the living environment and the problems they face in the living environment (17-18).

The Wechsler Intelligence Scale, Children-review form (WISC-R), is the primary of the tests used to determine the original abilities in children. This test consists of four subtests that measure different neurocognitive functions. These sub-groups are visual-spatial ability (picture completion block design and Object assembly), verbal conceptualization ability; this ability measures the concept of language functions and the use of abstract thinking (comprehension+ similarities + vocabulary), arranging ability; this test determines the ability to remember the visual and audible stimuli stored in short-term memory (digit span + Picture arrangement +coding). On the other hand, this test determines the person's ability to use the acquired knowledge to solve problems in social life (İnformation + arithmetic and vocabulary). The full intelligence section shows the overall level of intelligence covering all the features mentioned (19). It is noteworthy that the diabetic groups participating in the study are close to the lower limit of the normal intelligence level score and that there is no difference between them and the children in the 6-11 age group constituting the control group have a higher score than the children in the study group in the total intelligence score. It is another remarkable finding that diabetic children's general intelligence scores should be at the lower end of the normal intelligence level, which is in the range of dull-normal intelligence scores (Table 5,6).

In our study, there was no the statistically significant difference between the groups in terms of the Wechsler intelligence scale verbal intelligence, performance intelligence, and full intelligence score scores (Table 5,6) . The verbal intelligence of the WISC-R intelligence scale which as the gold standard of academic success, use to assesses the school, cultural environment, general knowledge level, abstraction, generalization, attention, reasoning, auditory memory and learning and reasoning ability. Test performance section uses to assess the visual attention, causal relation building, visual-motion-spatial coordination, and psychomotor speed. There was no the statistically significant difference between both diabetes groups in terms of neurocognitive functions evaluated by the test (Table.5,6)

Neuropsychological studies associated with intelligence are important in terms of the showing that a lot of the cognitive functions. Intelligence tests indicate that all of these functions work together to create a single experience. In this regard, intelligence tests are often applied to obtain information about cognitive functions.

Comparison of all sub-tests of WISC-R according to the frequency of hypoglycemia in the groups; in the group with children less than 5 years of age, there was a significant difference in visual-motion-spatial function measured only by the block design subtest. This finding is consistent with the results of the Bender-Gestalt test, suggesting that visual perception is impaired in children with the early diagnosis of diabetes mellitus. In the study by Hannonen et al. (3), there was no the statistically significant difference between the diabetes mellitus group with the severe hypoglycemic frequency, which compared to with the diabetes mellitus group and control group without hypoglycemic frequency in the term of the subgroups of the WISC-R intelligence scale. On the other hand, the results of the study conducted by

2016;23(1):36-41
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Hagen et al. do not support our results(20). in which they stated a significant shortening in early-onset diabetes mellitus group in the test of number subsequences, which measures the auditory short-term memory of the WISC-R intelligence scale. In this study, it is stated that children with diabetes mellitus, especially the early-onset diabetes mellitus group, often use wrong strategies to remember and organize information according to the control group.

In conclusion, it is seen that Type I diabetes affects recall memory in children negatively in terms of visual-spatial and visual-auditory stimuli. Therefore, early diagnosis and metabolic control are important in terms of preventing possible changes. However, it may be possible to prevent these children from falling back with their peers in term of their performances in their school and daily life by this method.

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