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Динамическое изменение перфузии головного мозга после когнитивной реабилитации у пациентов с сахарным диабетом 1 и 2 типа

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АННОТАЦИЯ

Введение. Результаты многочисленных исследований указывают на высокую распространенность когнитивных нарушений среди пациентов с сахарным диабетом (СД).

Цель. Оценить эффективность компьютеризированного тренинга в когнитивной реабилитации у лиц с СД 1 и 2 типа с учетом динамики перфузии головного мозга.

Материалы и методы. Рандомизированное контролируемое исследование. Исследуемую группу составили 25 пациентов с СД 1 типа и 30 пациентов с СД 2 типа в возрасте 23–67 лет. В группу сравнения вошли 20 пациентов с СД 1 типа (средний возраст 28,4 года) и 20 пациентов с СД 2 типа (средний возраст 56,0 лет). До и после курса реабилитации пациенты исследуемой группы прошли общеклиническое обследование, анализ крови на показатели углеводного обмена, тестирование когнитивных функций с использованием Монреальской шкалы (англ.: *Monreal Cognitive Assessment*, МоСА тест), бесконтрастную перфузионную магнитно-резонансную томографию (МРТ) головного мозга. Активная реабилитация продолжалась 6 месяцев, основывалась на компьютеризированном тренинге, включающем упражнения на вербальный и невербальный интеллект.

Результаты. На момент первичного обследования все исследуемые не имели достигнутого целевого уровня гликированного гемоглобина. После завершения программы тренинга удалось отметить снижение указанного показателя в обеих группах, а также снижение среднего уровня гликемии натощак у лиц с СД 1 типа. Результат нейропсихологического тестирования у всех пациентов на начальном этапе соответствовал диагнозу «когнитивная дисфункция». Контрольный тест выявил улучшение когнитивного статуса по общему баллу, шкале абстракции, речи, памяти и зрительно-конструктивных навыков. Корреляционный анализ в группе с СД 1 типа показал, что на результат выполнения упражнений на визуальное внимание и слуховое восприятие влияет функция памяти. У лиц с СД 2 типа повышенный гликированный гемоглобин ассоциировался со снижением когнитивных функций по общему баллу МоСА теста, а также в заданиях на речь, память, зрительно-конструктивные навыки. При динамическом анализе изменений МРТ-картины зарегистрирована гипоперфузия в зоне правого и левого таламуса у пациентов с СД 1 и 2 типа соответственно, а также усиление перфузии белого вещества правой теменной доли в группе с СД 1 типа и в области скорлупы слева у исследуемых в группе с СД 2 типа.

Заключение. У пациентов с СД 1 и 2 типа, а также с когнитивным дефицитом, прошедших курс когнитивной реабилитации с использованием компьютеризированного тренинга, удалось отметить улучшение когнитивного статуса, что подтверждалось результатами бесконтрастной перфузионной МРТ.

Ключевые слова: *сахарный диабет 1 и 2 типа; когнитивные функции; перфузия головного мозга; реабилитация*

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Dynamic Changes in Brain Perfusion after Cognitive Rehabilitation in Patients with Type 1 and Type 2 Diabetes Mellitus

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ABSTRACT

INTRODUCTION: The results of numerous studies indicate a high prevalence of cognitive impairment among patients with diabetes mellitus (DM).

AIM: To evaluate the effectiveness of computerized training in cognitive rehabilitation in individuals with type 1 and type 2 DM, taking into account the dynamics of brain perfusion.

MATERIALS AND METHODS: A randomized controlled study. The study group consisted of 25 patients with type 1 DM and 30 patients with type 2 DM aged 23 to 67 years. The comparison group included 20 patients with type 1 DM (mean age 28.4 years) and 20 patients with type 2 DM (mean age 56.0 years). Before and after the rehabilitation course, the patients of the study group underwent a general clinical examination, a blood test for carbohydrate metabolism, cognitive function testing using the Montreal Scale (MoCA test), contrast-free perfusion magnetic resonance imaging (MRI) of the brain. Active rehabilitation lasted 6 month; it was based on a computerized training, including exercises on verbal and nonverbal intelligence.

RESULTS: On the initial examination, all the subjects did not have the achieved target level of glycated hemoglobin. After completion of the training program, a decrease in the parameter in both groups was noted, as well as a decrease in the mean level of fasting glycemia in people with type 1 DM. The result of neuropsychological testing in all patients at the initial stage corresponded to the diagnosis of 'cognitive dysfunction'. The control test revealed an improvement in cognitive status according to the overall score, the abstraction scale, speech, memory and visual-constructive skills. Correlation analysis in the group with type 1 DM showed that the result of exercises on visual attention and auditory perception was influenced by memory function. In individuals with type 2 DM, increased glycated hemoglobin was associated with a decrease in cognitive functions according to the overall score of the MoCA test, as well as in tasks for speech, memory, visual-constructive skills. Dynamic analysis of changes in the MRI picture revealed hypoperfusion in the area of the right and left thalamus in patients with type 1 and type 2 DM, respectively, as well as increased perfusion of the white matter of the right parietal lobe in the group with type 1 DM, and in the putamen area on the left in the group with type 2 DM.

CONCLUSION: In patients with type 1 and type 2 DM, as well as with cognitive deficit, who underwent a course of cognitive rehabilitation using computerized training, an improvement in cognitive status was noted, which was confirmed by the results of contrast-free perfusion MRI. to evaluate the effectiveness of computerized training in cognitive rehabilitation in people with type 1 and type 2 diabetes mellitus, taking into account the dynamics of brain perfusion.

Keywords: *type 1 and type 2 diabetes mellitus; cognitive functions; brain perfusion; rehabilitation*

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ECO•VECTOR

LIST OF ABBREVIATIONS

CI — cognitive impairment
DM — diabetes mellitus
HbA1c — glycated hemoglobin
MoCA тест — Monreal Cognitive Assessment
MRI — magnetic resonance imaging

INTRODUCTION

Currently, the results of numerous studies indicate increased prevalence of cognitive impairment (CI) among patients with diabetes mellitus (DM) in comparison with healthy population. Cognitive dysfunction is a significant factor in limitation of self-care and working capacity in patients with DM [1]. The neuropsychological profile of patients with DM is characterized by a predominance of disorders in attention, speed of psychomotor reactions, verbal fluency, ability to switch between tasks, conceptual thinking, etc. [2].

In patients with type 2 DM, there was noted a statistically significant association of cognitive decline and decompensation of glycemic control with duration of the disease [3]. In a cross-sectional study of the brain neuroimaging and cognitive functions in 350 patients with type 2 DM, an impairment of visual-spatial construction, planning, visual memory and information processing speed was recorded irrespective of age, gender, educational background and vascular complications. Type 2 DM was associated with expansion of liquor-containing spaces and reduction of the total brain volume (atrophic alterations of the gray matter), mainly in the temporal, parahippocampal, cingulate gyri, precuneus, insular and medial frontal areas, and with signs of neurodegeneration of the subcortical gray matter in the caudate nucleus region and putamen. The gray matter atrophy was more pronounced in the left hemisphere, while morphometric alterations of the white matter were found primarily in the frontal and temporal lobes [4].

A prolonged course of type 1 DM is also associated with the reduction of cognitive abilities regardless of other complications of the disease [5]. Middle-aged adults with a long standing type 1 DM had a partial lesion of the white matter and reduction of the fractional anisotropy index in the posterior parts of the brain. In a study with use of a single-photon emission tomography conducted in patients with type 1 DM, significant differences in cerebral perfusion were documented in many regions and were most pronounced in the cerebellum, frontal and fronto-temporal lobes. These alterations were associated with a poor glycemic control and microvascular complications [6].

A meta-analysis of six randomized controlled studies (16,584 participants) showed that intensive glucose control in patients with type 2 DM can slow down the deterioration of cognitive functions, especially impairment of memory [7]. According to the results of the ACCORD-MIND cohort study (the Action to Control Cardiovascular Risk in Diabetes Memory in Diabetes), strict glycemic control in elderly patients with type 2 DM at a high cardiovascular risk, did not contribute to the correction of CI and improvement of the results of magnetic resonance imaging (MRI) of the brain due to a variety of comorbid conditions [8]. Therefore, optimal glycemic control in type 1 DM and the identification of risk factors, as well as the use of a preventive approach, are essential to prevent the development of cognitive insufficiency.

More and more attention is being paid to cognitive rehabilitation based on training with the use of digital technologies. Computerized training is effective and has a multicomponent mechanism of action, since it contributes both to the improvement of the cognitive profile of patients, primarily of the elderly ones, and to the long-term improvement of daily activity [9].

Due to the increasing frequency of cognitive dysfunction as a DM complication, it is necessary to search for methods of rehabilitation sensitive to both conditions.

The **aim** of this study to evaluate the effectiveness of computerized training in cognitive rehabilitation of individuals with types 1 and 2 diabetes taking into account the dynamics of brain perfusion.

MATERIALS AND METHODS

The protocol of the study was considered and approved by Ethics Committee of Siberian State Medical University (Protocol No. 5265 of May 02, 2017). Each patient provided a written informed consent.

The design of study a simple randomized controlled study. Patients were randomly selected using a random number table.

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Inclusion criteria: patients diagnosed with type 1 or type 2 DM (the age was from 23 to 67 years); the duration of the disease, the level of glycemia, the presence/absence of complications and the type of therapy were not taken into account when forming the sample.

Exclusion criteria: use of medical drugs/substances that stimulate or suppress cognitive functions; chronic heart failure above II functional class or in decompensation stage, acute coronary syndrome and transitory ischemic attack in the previous 6 months, contraindications to brain MRI, organic brain lesions.

The *main study group* included 25 patients with type 1 DM aged 29.8 (25.3–30.0) years and 30 patients with type 2 DM aged 58.5 (46.0–66.5) years. The *comparison group* included 20 patients with type 1 DM and 20 patients with type 2 DM, the mean age 28.4 (23.5–31.5) and 56.0 (49.0–62.5) years, respectively, who were followed up but did not undergo rehabilitation measures.

Each participant was assigned an individual number and underwent a common clinical examination, a blood test for glycemia and glycated hemoglobin (HbA1c), tests for cognitive functions on Monreal scale (Monreal Cognitive Assessment MoCA), perfusion MRI of the brain. MRI was performed on a 1.5 T Signa Creator E tomograph (GE Healthcare, China). Non-contrast brain perfusion was performed by using the arterial spin labeling technique, field of view 250 mm, matrix 64 x 64, repetition time 2 500, echo time 12.0, number of scan repetitions 1, slice thickness 8 mm. In the reference regions, dimensions of the area of interest were outlined in such a way as not to involve large vessels (arteries and veins).

Before being included in the groups, the patients were tested using the Russian universal questionnaire for quantitative evaluation of adherence to treatment (Rus. КОП-25). All the patients had a high level of adherence — 75% and above. Active rehabilitation lasted 6 months, and in the next 6 months, the control of the effectiveness, determination of the time of end result and correction of the disorders were conducted.

For cognitive rehabilitation, a computerized training based on the Scientific brain training digital platform (HAPPYNeuronPro) was used, consisting of 8 modules of exercises for verbal and nonverbal intelligence (spatial memory, visual memory, information processing speed, executive functions, etc.). At the beginning of the study, a personal area was created for each patient with instructions on navigation in the program. The training was conducted twice a week, with the duration of one session 45 minutes.

After completion of the rehabilitation program, all the subjects underwent repeated blood sampling, neuropsychological testing and non-contrast perfusion MRI.

Five patients with type 1 diabetes were excluded from the sample due to the failure to adjust to the training schedule. Currently, the patients are on follow-up until the end of the study. The patients were warned about using only hypoglycemic therapy during the study and not any other therapy (which might affect changes in brain perfusion), and to report all new appointments from the attending physician or other specialists to the center for registration.

During the study, no use of medications that could significantly affect the results of the study was reported.

For statistical evaluation of the data obtained, a Russian version of IBM SPSS Statistics 19.0.0 analytical software (IBM SPSS Inc., USA) was used. The normality of the distribution of the variable was checked using Shapiro–Wilk W-test, the normal distribution — using Student's t-test. Unrelated samples were compared using Mann–Whitney U-test. The calculation of the arithmetic mean and the error of mean were used as descriptive statistics. The critical significance level (p) when testing statistical hypotheses in the study was assumed to be 0.05. Spearman's coefficient (r) was used to assess the correlation dependence of the parameters.

RESULTS

All the patients with type 1 DM were of young age and were comparable in gender. On the initial examination, the mean HbA1c level in the group of type 1 DM was 7.9%. In 6 months after the completion of the training program, HbA1c level reduced by 0.7%. The mean fasting glycemia level before and after rehabilitation was 9.6 and 8.0 mmol/l, respectively. The comparison group were patients with comparable parameters before the rehabilitation; with no significant differences in the parameters after the follow-up period (Table 1).

At the initial stage, the result of neuropsychological testing corresponded to the diagnosis ‘cognitive dysfunction’ (score < 26). In both groups, functions on the memory (main: $U = 38.0$, $p = 0.000002$; control: $U = 142.5$, $p = 0.04$), and on the attention scale (main: $U = 56.0$, $p = 0.000002$; control: $U = 92.5$, $p = 0.03$) were reduced (Table 2).

The control neuropsychological test in the main group revealed an improvement of the cognitive status according to the total score, the abstraction scale, in speech, memory and visual-constructive skills. In addition, memory function influenced the result of performing visual attention and auditory perception exercises ($r = 0.5$, $p = 0.03$; $r = 0.54$, $p = 0.02$). There were no significant changes in the comparison group.

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Table 1. Characteristics of Patients with Type 1 Diabetes Mellitus, Parameters of Carbohydrate Metabolism before and after Rehabilitation

Parameters	Patients with Type 1 DM, Main Group	Patients with Type 1 DM, Comparison Group
n	25	20
Age, years	29.8 (25.3–30.0)	28.4 (23.5–31.5)
Duration of type 1 DM, years	13.5 (8.4–20.0)	11.5 (7.8–18.0)
Gender, male/female, % (n)	58.0 (11)/42.1 (8)	60.0 (12)/40.0 (8)
Mean HbA1c level, % (before rehabilitation/follow-up)	7.9 (6.0–9.3)	7.5 (6.2–9.0)
Mean glycemia level, mmol/l (before rehabilitation/follow-up)	9.6 (7.4–10.6)	9.8 (7.2–11.5)
Mean HbA1c level, % (after rehabilitation/follow-up)	7.2 (5.9–8.8)	7.6 (6.4–9.1)
Mean glycemia level, mmol/l (after rehabilitation/follow-up)	8.0 (6.9–9.3)	9.5 (7.0–11.1)

Notes: type 1 DM — type 1 diabetes mellitus; HbA1c — glycated hemoglobin

Table 2. Cognitive Function on Montreal Scale in Patients with Type 1 Diabetes Mellitus before and after Rehabilitation Course

Tasks	Patients with Type 1 DM, Main Group		Patients with Type 1 DM, Comparison Group	
	before rehabilitation	after rehabilitation	before follow-up	after follow-up
n	25	25	20	20
Total score	24.5 (23.0–28.0)	***27.0 (26.5–27.5)****	25.0 (23.0–28.0)	24.5 (23.0–28.0)
Visual-constructive skills	3.5 (3.0–4.5)	***4.5 (4.0–5.0)****	4.0 (3.0–4.5)	3.5 (3.0–4.5)
Naming	3.0 (3.0–3.0)	3.0 (3.0–3.0)	3.0 (3.0–3.0)	3.0 (3.0–3.0)
Attention	5.5 (6.0–6.0)	5.5 (6.0–6.0)	5.5 (6.0–6.0)	5.5 (6.0–6.0)
Speech	2.0 (2.0–3.0)	***2.5 (2.0–3.0)****	2.0 (2.0–3.0)	2.0 (2.0–3.0)
Abstraction	1.5 (1.0–2.0)	***2.0 (2.0–2.0)****	1.5 (1.0–2.0)	1.5 (1.0–2.0)
Memory	3.0 (3.0–4.0)	***3.5 (3.0–4.0)****	3.0 (3.0–4.0)	3.0 (3.0–4.0)
Orientation	6.0 (6.0–6.0)	6.0 (6.0–6.0)	6.0 (6.0–6.0)	6.0 (6.0–6.0)

Note: * — $p < 0.05$; type 1 DM — type 1 diabetes mellitus

In the dynamic analysis of the brain perfusion, hypoperfusion of the right thalamus area ($p = 0.01$) and increased perfusion of the white matter of the right parietal lobe ($p = 0.03$) were recorded after rehabilitation in the group with type 1 diabetes (Table 3).

When studying the dynamics of non-contrast perfusion, no changes were identified in the comparison group.

When assessing the parameters of carbohydrate metabolism of the main group with type 2 diabetes (n = 30), at the initial stage, the average level of HbA1c exceeded the target level — 7.6%. After a rehabilitation course, the parameter declined to 6.9%. Here, the patients from the comparison group were comparable, and after the follow-up period, a mild increase in the level of glycemia and HbA1c was noted (Table 4).

Table 3. Dynamics of Results of Non-Contrast Perfusion Using Arterial Spin Labeling Technique in Patients with Type 1 Diabetes Mellitus before and after Rehabilitation

Cerebral Circulation, ml/100 g/min	Before Rehabilitation	After Rehabilitation	p
Right lobe, gray matter	76.4 ± 15.5	62.2 ± 13.3	0.44
Left lobe, gray matter	58.8 ± 17.2	60.4 ± 9.3	0.15
Right frontal lobe, white matter	28.4 ± 6.8	44.2 ± 12.7	0.41
Left frontal lobe, white matter	29.4 ± 9.9	33.0 ± 5.1	0.29
Right parietal lobe, gray matter	73.6 ± 24.2	69.8 ± 18.8	0.68
Left parietal lobe, gray matter	67.6 ± 19.3	79.4 ± 13.6	0.37
Right parietal lobe, white matter	35.0 ± 11.7	31.8 ± 5.6	***0.03****
Left parietal lobe, white matter	39.6 ± 9.7	33.8 ± 10.7	0.58
Right occipital lobe, gray matter	74.8 ± 28.9	74.8 ± 24.7	0.66
Left occipital lobe, gray matter	69.2 ± 20.9	60.4 ± 10.1	0.07
Right occipital lobe, white matter	37.0 ± 15.7	42.6 ± 12.5	0.80
Left occipital lobe, white matter	37.4 ± 12.7	36.4 ± 7.8	0.54
Right temporal lobe, gray matter	47.2 ± 10.5	51.0 ± 8.6	0.82
Left temporal lobe, gray matter	44.6 ± 25	63.4 ± 18.3	0.3
Right temporal lobe, white matter	43.0 ± 9.4	41.4 ± 6.4	0.71
Left temporal lobe, white matter	36.0 ± 10.5	42.4 ± 7.1	0.3
Right putamen	43.8 ± 6.6	42.2 ± 10.5	0.37
Left putamen	40.8 ± 8.0	37.0 ± 5.4	0.67
Right amygdala	47.8 ± 8.6	52.0 ± 6.1	0.49
Left amygdala	44.8 ± 10.8	51.6 ± 10.5	0.93
Right head of caudate nucleus	53.2 ± 16.2	55.2 ± 8.4	0.39
Left head of caudate nucleus	51.6 ± 14.6	50.8 ± 13.7	0.77
Right pale globe	36.4 ± 6.3	28.6 ± 4.9	0.38
Left pale globe	34.8 ± 6.3	28.6 ± 4.9	0.42
Right thalamus	77.2 ± 15.6	61.6 ± 6.9	***0.01****
Left thalamus	64.2 ± 20.8	59.2 ± 9.1	0.35

Note: * — $p < 0.05$

All the subjects had cognitive deficit, that is, the total score was below 26. The most significant reduction was noted on the scales of visual-constructive skills, speech, abstraction and memory. Control testing in the main group revealed a significant improvement of cognitive functions in the total score, on the scales of naming, speech, abstraction and memory. The results of the comparison group did not show any significant changes (Table 5).

A positive correlation relationship was identified between a high level of HbA1c and cognitive disorders in the total MoCA score ($r = -0.41$, $p = 0.04$), in the tasks for speech ($r = -0.33$, $p = 0.0003$), memory ($r = -0.39$, $p = 0.04$), visual-constructive skills ($r = 0.36$, $p = 0.05$).

In patients with DM 2, the following alterations in the neuroimaging of the brain were found: a pronounced reduction of perfusion of the left thalamus ($p = 0.01$) and enhancement in the putamen area on the left ($p = 0.03$, Table 6).

Table 4. Characteristics of Patients with Type 2 Diabetes Mellitus, Parameters of Carbohydrate Metabolism before and after Rehabilitation

Parameters	Patients with DM Type 2, Main Group	Patients with DM Type 2, Comparison Group
n	30	20
Age, years	58.5 (46.0–66.5)	56.0 (49.0–62.5)
Duration of DM 2, years	5.5 (2.0–8.5)	6.0 (2.0–9.0)
Gender, male/female, % (n)	26.7 (8)/73.3 (22)	56.7 (17)/43.3 (13)
Mean HbA1c level, % (before rehabilitation/follow up)	7.6 (6.7–8.4)	6.9 (6.2–7.6)
Mean glycemia level, mmol/l (before rehabilitation/follow up)	8.5 (6.4–9.0)	6.6 (5.9–7.5)
Mean HbA1c level, % (after rehabilitation/follow up)	6.9 (6.2–8.0)	6.8 (6.0–7.8)
Mean glycemia level, mmol/l (after rehabilitation/follow up)	6.7 (6.1–7.8)	7.0 (6.2–7.3)

Notes: DM 2 — type 2 diabetes mellitus; HbA1c — glycated hemoglobi

Table 5. Cognitive Function on Montreal Scale in Patients with Type 2 Diabetes Mellitus before and after Rehabilitation Course

Task	Patients with DM 2, Main Group		Patients with DM 2, Comparison Group	
	before rehabilitation	after rehabilitation	before follow-up	after follow-up
n	30	30	20	20
Total score	20.0 (18.0–27.0)	***25.0 (21.0–28.0)****	21.0 (18.0–27.0)	21.0 (18.0–27.0)
Visual-constructive skills	3.0 (2.0–4.0)	***3.5 (3.0–4.0)***	3.0 (2.0–4.0)	3.0 (2.0–4.0)
Naming	2.0 (3.0–3.0)	3.0 (3.0–3.0)*	3.0 (3.0–3.0)	3.0 (3.0–3.0)
Attention	4.5 (4.0–6.0)	5.0 (5.0–6.0)	4.5 (4.0–6.0)	4.5 (4.0–6.0)
Speech	1.5 (1.0–2.0)	***2.5 (2.0–3.0)****	1.5 (1.0–2.0)	1.5 (1.0–2.0)
Abstraction	1.0 (0–2.0)	***2.0 (2.0–2.0)****	1.0 (0–2.0)	1.0 (0–2.0)
Memory	2.0 (1.0–4.0)	***3.0 (2.0–4.0)****	2.0 (1.0–4.0)	2.0 (1.0–4.0)
Orientation	6.0 (6.0–6.0)	6.0 (6.0–6.0)	6.0 (6.0–6.0)	6.0 (6.0–6.0)

Notes: * — $p < 0.05$; DM 2 — type 2 diabetes mellitus

In patients with DM2 of the comparison group no changes in perfusion were found.

According to the results of a survey of participants about satisfaction with the process of computerized cognitive rehabilitation, 90% of participants gave a positive answer and agreed to continue the course. The reasons for the refusal of training in the remaining patients were lack of time (n = 8) and difficulties in performing exercises (n = 2).

Table 6. Dynamics of Results of Non-Contrast Diffusion Using Arterial Spin Labeling Technique in Patients with Type 2 Diabetes Mellitus before and after Rehabilitation

Cerebral Blood Flow, ml/100 g/min	Before Rehabilitation	After Rehabilitation	p
Right lobe, gray matter	9.8 ± 8.1	60.7 ± 18.0	0.21
Left lobe, gray matter	12.0 ± 8.8	57.5 ± 16.3	0.41
Right frontal lobe, white matter	13.2 ± 9.3	38.0 ± 10.2	0.72
Left frontal lobe, white matter	13.8 ± 9.5	33.0 ± 8.5	0.58
Right parietal lobe, gray matter	12.8 ± 11.8	72.5 ± 16.0	0.32
Left parietal lobe, gray matter	12.0 ± 8.6	68.5 ± 13.5	0.77
Right parietal lobe, white matter	12.5 ± 8.9	31.2 ± 6.5	0.56
Left parietal lobe, white matter	11.0 ± 8.2	34.5 ± 8.9	0.85
Right occipital lobe, gray matter	6.5 ± 2.3	54.7 ± 9.5	***0.03****
Left occipital lobe, gray matter	10.8 ± 9.0	52.7 ± 18.5	0.27
Right occipital lobe, white matter	12.0 ± 9.6	36.8 ± 8.8	0.86
Left occipital lobe, white matter	12.7 ± 9.2	30.7 ± 11.8	0.46
Right temporal lobe, gray matter	15.2 ± 11.2	40.1 ± 11.2	0.86
Left temporal lobe, gray matter	37.3 ± 14.8	44.0 ± 4.5	0.26
Right temporal lobe, white matter	12.0 ± 8.6	32.8 ± 14.8	0.28
Left temporal lobe, white matter	14.2 ± 9.3	37.8 ± 11.2	0.77
Right putamen	20.8 ± 14.7	44.2 ± 14.1	0.53
Left putamen	21.0 ± 15.9	40.8 ± 8.3	***0.03****
Right amygdala	21.8 ± 17.7	46.8 ± 10.4	0.08
Left amygdala	29.3 ± 25.3	46.3 ± 12.4	0.06
Right head of caudate nucleus	25.0 ± 25.3	56 ± 12.3	0.05
Left head of caudate nucleus	20.7 ± 11.7	48.5 ± 10.8	0.68
Right pale globe	21.3 ± 16.8	34.5 ± 10.3	0.12
Left pale globe	23.7 ± 22.0	33.3 ± 11.5	0.32
Right thalamus	25.8 ± 21.4	44.3 ± 19.7	0.47
Left thalamus	117.8 ± 184.1	42.8 ± 10.3	***0.01****

Note: * — $p < 0.05$

DISCUSSION

According to the data of the Swedish National Diabetes Register (378,299 patients with DM 2), the risk of vascular dementia and probability for Alzheimer disease in patients with HbA1c levels > 10.1% was higher by 93% and 34%, respectively, compared to patients with HbA1c levels < 6.9% [10]. In our study, all the patients with DM had a deficit of cognitive functions. In the subjects with DM 2, the highest deficit was in the parameters of visual-constructive skills, speech, abstraction and memory, and in patients with DM 1 in the parameters of attention and memory. Correlation analysis in the DM 1 group showed the effect of the memory function on the result of exercises for visual attention and auditory perception. Besides, a positive correlation relationship has been established between a high level of HbA1c and a cognitive dysfunction in the total MoCA test score, and in the tasks for speech, memory, visual-constructive skills.

Currently, digital technologies are being widely applied in cognitive rehabilitation [11]. Elderly people with an increased risk of dementia due to DM demonstrated improvements in both intellectual activity and self-control of the disease after computerized cognitive training at home [12]. In another study, cognitive rehabilitation resulted in improvement of cognitive abilities specific to the abilities trained, compared with the control group, which continued 5 years after the initiation of the intervention [13]. Australian scientists have shown a positive effect of 30-minute daily sessions during a month of computerized cognitive training of attention, speed of cognitive functions, visual memory and executive functions in elderly patients with moderate cognitive disorders [14]. Our results agree with previous studies. After 6 months of cognitive rehabilitation, the parameters of neuropsychological testing in patients with type 1 and type 2 diabetes improved.

Disorders of cerebral perfusion are often put forward as a cause of cognitive deficit in patients with DM. An evident association is shown between hypoperfusion of the caudal part of the cingulate gyrus and precuneus and a cognitive deficit in patients with DM 2 [15]. A decrease in the blood flow velocity in the white and gray matter area of the frontal, occipital, temporal lobes and putamen has been documented in patients with type 1 diabetes and cognitive dysfunction [16]. There is an assumption that cognitive training enhances neuronal activity increasing blood supply to these regions through nervovascular coupling [17]. The dynamic analysis of perfusion after a computerized cognitive training session showed enhanced perfusion of the white matter of the right parietal lobe in patients with DM 1, and in the putamen region on the left in patients with DM 2, *which evidences importance of neurocognitive training in improvement of perfusion of some regions of the brain*. However, in both types of DM, hypoperfusion of the right thalamus and evident hypoperfusion of the left thalamus were recorded in cognitive rehabilitation. We assign these results to certain factors. Thus, it has been shown that a multidisciplinary approach, additional use of exercises, permits to reduce cognitive deficit and to improve the brain hemodynamics [18, 19]. Another likely mechanism is a probable development of thalamic dementia which resembles CI in DM and is associated with such risk factors as arterial hypertension, dyslipidemia, etc. [20].

CONCLUSION

Patients with diabetes mellitus are at high risk of cognitive decline. The primary or diabetes-induced cognitive dysfunction negatively affects patients' self-control, leading to the development or progression of complications and impairment of quality of life. This evidences the need to define them as a target group for prophylaxis.

In patients with type 1 and type 2 diabetes mellitus and with cognitive deficit, who underwent a course of cognitive rehabilitation using computerized training based on the Scientific brain training digital platform (HAPPYNeuronPro), an improvement in cognitive status was noted, which was confirmed by contrast-free perfusion magnetic resonance imaging.

Thus, it is essential to improve specialized cognitive training programs for training the speed of information processing, attention, short-term memory, executive functions, verbal and visual-spatial skills, and to use them in the development of prevention and rehabilitation measures in treatment of diabetes mellitus.

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