Patient-Centered Approaches to Medical Intervention

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Cognitive Impairments and Neuroimaging Features in Type 2 Diabetes Mellitus

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Abstract
Type 2 diabetes mellitus (T2DM) is a prevalent chronic condition, and cognitive dysfunction is increasingly recognised as a complication, partly due to longer life expectancy resulting from improved disease management. This study aimed to examine the neuroimaging characteristics of cognitive impairment in T2DM and its relationship with blood glycaemic parameters. Sixty patients with T2DM were assessed using the Montreal Cognitive Assessment (MoCA) and the McNair and Kahn scales. Brain MRI was performed with GE Optima 450w 1.5T, following standard protocols. The results showed cognitive dysfunction in all patients with chronic cerebral ischemia, with MRI data revealing reduced hippocampal, grey, and white matter volumes. These findings suggest that brain atrophy, particularly in the white and grey matter and hippocampus, is common in T2DM patients, especially those with chronic cerebral ischemia. This atrophy is closely linked to glycaemic variability, highlighting the need for monitoring in diabetic care.

Keywords: magnetic resonance imaging, type 2 diabetes mellitus, glycemia, glycated hemoglobin, chronic cerebral ischemia, cognitive dysfunction, leukoreosis

Introduction
Type 2 Diabetes Mellitus (T2DM) is a prevalent metabolic disorder that affects millions globally and is associated with various complications, including cognitive dysfunctions. Cognitive impairments in T2DM, particularly in memory, attention, and executive functions, have been observed in numerous studies. Neuroimaging techniques, such as MRI, have provided crucial insights into brain structure alterations associated with T2DM-related cognitive dysfunctions, revealing reductions in white and grey matter volumes and cortical thickness in regions such as the hippocampus and frontal cortex[1]. Additionally, studies have highlighted the role of cerebrovascular abnormalities, including microvascular damage and atherosclerosis, in exacerbating these impairments, which contribute to the progression of cognitive decline[2]. Glycemic variability has also been linked to these neurodegenerative changes, indicating a complex interplay between metabolic control and brain health[3]. With the growing recognition of the impact of T2DM on cognitive functions, the current study seeks to explore neuroimaging characteristics and their association with blood glycemic parameters. Understanding these connections can aid in developing targeted interventions that not only manage T2DM but also mitigate its cognitive consequences, offering significant advancements in medical science. Our aim is to assess the neuroimaging characteristics of cognitive impairment in T2DM in relation to blood glycemic parameters.

Materials and methodology
In this study, 60 patients (28 men, 32 women) with Type 2 Diabetes Mellitus (T2DM) were recruited from the endocrinology department for a neuroimaging and cognitive function analysis. The Montreal Cognitive Assessment (MoCA) was employed as a neuropsychological tool to evaluate various cognitive domains, including memory, attention, executive functions, and language skills, with scores below 26 indicating cognitive dysfunction. Additionally, the McNair and Kahn scale was used for self-assessment of memory, where a score above 42 signified cognitive issues.
Magnetic Resonance Imaging (MRI) was performed on all patients using the GE Optima 450w 1.5T system to detect brain abnormalities, focusing on hippocampal and white/grey matter volumes. Standard MRI sequences like T1-SE sag, T2-SE cor-tra, T2-FLAIR tra, and DWI tra (5mm) were used for comprehensive brain imaging. Laboratory markers such as glycated haemoglobin (HbA1c) and blood glucose levels were measured on the first day of hospitalization to assess glycemic control.
Inclusion criteria were adults with a confirmed diagnosis of T2DM, while exclusion criteria excluded those with other neurodegenerative diseases, psychiatric disorders, or severe comorbidities that could confound cognitive or imaging results.

Results
The study included 60 patients with type 2 diabetes mellitus, aged between 43 and 75 years, comprising 28 men and 32 women. These patients were divided into two equal groups of 30 based on the presence or absence of chronic cerebral ischemia (CCI) and cognitive impairment. The average age of patients in the first group, who had CCI, was 55.25±0.78 years, while in the second group, it was 53.5±0.94 years. Additionally, the duration of diabetes in the first group was longer, with an average of 13.45±1.43 years. Detailed characteristics of the study participants are presented in Table 1.

Table 1. Characteristics of patients of the first and second groups

Index	Group 1 Type 2 DM + CCI (n=30)	Group 2 Type 2 DM without CCI (n=30)	p-value
Age, years	55,25±0.78	53,5±0.94	p≤0,0001
Gender, male/female	13/17	15/15	-
Duration of T2DM, years	13,45±1.43	10,2±0.57	p≤0,0001

In the first group, which included patients with type 2 diabetes and chronic cerebral ischemia, the average score on the Montreal Cognitive Assessment (MoCA) questionnaire was 21.2±0.86 points, ranging from 15 to 26 points. Cognitive dysfunction was evident in all patients from this group. Similar findings were noted in the self-assessment of memory using the McNair and Kahn scales, where the average score was 45.6±0.78, with a range of 43 to 54 points, further indicating cognitive impairment. In contrast, the second group, consisting of individuals with type 2 diabetes but without chronic cerebral ischemia, showed normal cognitive function. Their MoCA scores were within the normal range (≤26 points), and the McNair and Kahn scale also reflected normal memory function (≥42 points). Detailed results are presented in Table 2.

Table 2. **Average Cognitive Status Scores in All Patients**

Index	Group 1 Type 2 DM + CCI (n=30)	Group 2 Type 2 DM without CCI (n=30)	p-value
MoCA, total score	21,2±0.86	27,3±0.65	p≤0,0001
McNair & Kahn Scale	45,6±0,78	34.9±1,76	p≤0,0001

Glycated haemoglobin (HbA1c, %) and blood glucose levels (mmol/L), measured on the first day of hospitalization, were used as laboratory markers. In the study group, patients with chronic cerebral ischemia and type 2 diabetes exhibited higher levels of blood carbohydrate metabolism.

Table 3. **Average blood glycemic parameters of patients**

Index	Group 1 Type 2 DM + CCI (n=30)	Group 2 Type 2 DM without CCI (n=30)	p-value
HbA1c, %	8,12±0.67	7,2±0.75	p≤0,0001
Glycemia, mmol/L	7,9±0.97	6,9±0.96	p≤0,0002

To assess the neuroimaging features of cognitive impairment, MRI data from patients in both groups were analysed. Focal changes in white matter were found in 25 patients (83.3%) in group 1 and in 8 patients (26.6%) in group 2 (P<0.05). Leukoaraiosis was observed in 22 patients (73.3%) in group 1 and in 7 patients (23.3%) in group 2 (P<0.001), located in the posterior and anterior periventricular regions, often forming a rim around the entire periventricular area. Lateral ventricular dilation was noted in 26 patients (86.6%) in group 1 and in 10 patients (33.3%) in group 2 (P<0.03). Pronounced deepening of the hemispheric sulci was observed in 27 patients (90%) in group 1 and in 6 patients (20%) in group 2 (P<0.002).

Table 4. **Frequency of detection of structural changes in the brain in individuals with T2D according to MRI data**

Indicators	Group 1 Type 2 DM + CCI (n=30)		Group 2 Type 2 DM without CCI (n=30)	
	Abs	%	Abs	%
Focal white matter changes	25	83,3	8	26,6*
Leukoareosis	22	73,3	7	23,3***
Dilation of the lateral ventricles	26	86,6	10	33,3*
Pronounced deepening of the hemispheric sulci	27	90	6	20**

Note: - differences relative to group 1 are significant (* - P<0.05, ** - P<0.01, *** - P<0.001

In patients with type 2 diabetes and chronic cerebral ischemia, a reduction in the volume of the hippocampus, as well as the grey and white matter, was observed (Table 4).

Table 4. Indicators of brain morphometry in patients of the first and second groups, mm 3

Anatomical Area	Group 1 Type 2 DM + CHEM (n=30)	Group 2 Type 2 DM without CCI (n=30)
Gray matter of the brain,	474 655,34	565 297,50
Left hemisphere	255 582,41	356 189,76
Right hemisphere	256 582,93	309 678,81
The white matter of the brain,	467 598,50	667 765,79
Left hemisphere	245 501,10	315 786,08
Right hemisphere	238 610,67	334 167,98
Hippocampus: left right	 71,59 72,45	 73,65 74,47

The glycemic lability index was significantly correlated with a reduction in hippocampal volume (r = -0.694, p = 0.03). Additionally, with increasing patient age, there was a more pronounced decline in grey matter volume (r = -0.9, p ≤ 0.001) and white matter volume (r = -0.8, p ≤ 0.001).

Discussion

Earlier studies investigating brain tissue in individuals with type 2 diabetes (T2DM) have reported various findings, including cortical and subcortical shrinkage, the presence of symptomatic or asymptomatic infarctions, and associations with white matter lesions in regions surrounding the brain's ventricles and beneath the cortex [4]. Meta-analyses have also identified significant reductions in overall brain volume, particularly in areas such as the orbitofrontal cortex, hippocampus, and basal ganglia [5]. However, conflicting results have emerged regarding the volumes of the frontal and temporal lobes, anterior cingulate, superior temporal, and parietal regions, as noted in other research [6].

Both cross-sectional and longitudinal studies using brain MRI have consistently shown a connection between diabetes mellitus (DM) and cerebral atrophy, especially affecting the hippocampus and amygdala. Additionally, these studies have demonstrated a strong association between diabetes and ischemic strokes, with cortical and subcortical microinfarctions being prevalent. Severe hypoglycemia has also been found to damage specific brain regions, notably the cortex and hippocampus [7]. Several pathophysiological hypotheses have been proposed to explain the increased risk of dementia in individuals with diabetes, with microinfarctions being a key factor linked to blood glucose fluctuations or microvascular changes caused by hyperglycemia [8]. Through our research on cognitive dysfunctions and neuroimaging characteristics in patients with T2DM, we have established significant associations between diabetes and impaired cognitive function. Neuroimaging findings consistently indicate structural and functional abnormalities in various brain regions, particularly affecting executive functions, attention and memory. Neuroimaging techniques such as MRI have proven instrumental in identifying and quantifying the structural and functional brain alterations in individuals with diabetes.

Conclusion

In conclusion, this study demonstrated that patients with Type 2 Diabetes Mellitus (T2DM) and chronic cerebral ischemia (CCI) experience significant cognitive dysfunctions and structural brain changes, particularly in the hippocampus, grey, and white matter. The findings revealed that higher glycemic variability and longer diabetes duration are associated with greater brain atrophy and cognitive decline. Neuroimaging techniques, such as MRI, were instrumental in identifying these structural abnormalities, including focal white matter changes, leukoaraiosis, and lateral ventricular dilation, all of which were more pronounced in patients with CCI. The results prove the importance of routine cognitive and neuroimaging assessments in T2DM patients, especially those with prolonged diabetes and poor glycemic control. Future research should focus on developing therapeutic strategies that address both glycemic variability and brain health. Additionally, further studies are needed to explore the potential for early interventions aimed at slowing or preventing cognitive decline in this population, offering new avenues for improving the quality of life for individuals with T2DM.

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Note: All the tables in this chapter were made by the author.