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RESEARCH ARTICLE

Impact of type 2 diabetes mellitus on short term and working memory

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ABSTRACT

Background: The increase in diabetes among the elderly is of concern because in addition to the wide range of traditional diabetes complications; evidence has been growing that diabetes is associated with increased risk of cognitive decline. **Aims and Objectives:** Aims and objectives of the study were to find out if there is any association between cognitive function and diabetes. **Materials and Methods:** The study was conducted in 200 individuals aged between 40 and 65 years consisting of 100 diagnosed cases of type 2 diabetics and 100 age and gender matched nondiabetics from outpatient department of McGann Hospital, Shimoga. Short term and working memory were assessed using neuropsychologial tests. Statistical analysis was performed using SPSS 21. **Results:** Scores of all the memory tests in type 2 diabetics were significantly reduced ($P < 0.001$) when compared to the memory scores of age and gender matched nondiabetics. **Conclusion:** The decreased memory status in type 2 diabetics may be due to many factors such as hyperglycemia, hypoglycemia, vascular disease, insulin resistance, and amyloid deposition.

KEY WORDS: Short Term Memory; Type 2 Diabetes; Working Memory

INTRODUCTION

Memories are stored in the brain by changing the basic sensitivity of synaptic transmission between neurons as a result of the previous neural activity. The new or facilitated pathways are called memory traces. They are important because once the traces are established; they can be selectively activated by the thinking mind to reproduce the memories.[1]

Memory function includes registration (encoding or acquisition), retention (storage or consolidation), stabilization and retrieval (decoding or recall). Registration and retrieval are conscious processes. Encoding process is dependent on the frontal lobes and hippocampal complex while retrieval requires the frontal lobes.[2]

Short-term memory refers to the function that temporarily retains stimuli that have just been perceived and lasts for ~20 sec. Working memory is a short-term memory system that allows concurrent retention and manipulation. It is used for thinking about what are already known and deriving conclusions on the basis of that knowledge.[3]

The deleterious effects of diabetes mellitus on the retinal, renal, cardiovascular, and peripheral nervous systems are widely acknowledged. Less attention has been given to the effect of diabetes on cognitive function. Neurological consequences of diabetes appear parallel to those observed in aging brain. The main hypothesis to explain the pathophysiology of cognitive decline associated with diabetes involves hyperglycemia, hypoglycemia, microvascular injury, insulin resistance, hyperinsulinemia, hyperphosphorylation of tau protein, and amyloid-β_2 deposition.[4]

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Hence, this study was conducted to evaluate the short term and working memory in type 2 diabetics and compare it with age and gender matched nondiabetics.

MATERIALS AND METHODS

The study was conducted in 200 individuals aged between 40 and 65 years consisting of 100 diagnosed cases of type 2 diabetes mellitus (DM) and 100 nondiabetics from outpatient department of McGann Hospital, Shimoga.

Institutional Ethical Committee clearance was obtained. Details of the study protocol were explained to the subjects who volunteered for the study, and Informed consent was taken; general information, present complaints, history of diabetes and hypertension if present, duration and treatment of same, any past illness, drug history, and family history were noted. Pulse and blood pressure were recorded. Laboratory investigations include fasting blood sugar and postprandial blood sugar.

Inclusion Criteria for Both the Groups

1. Age 40-65 years who have given written consent
2. Educational status: Minimum primary school.

Exclusion Criteria for Both the Groups

1. History of any known psychiatric disorders
2. History of any other known endocrinal disorders
3. History of any sedative/narcotic abuse
4. History of any other known medical disorders causing dementia
5. History of intake of any drugs known to cause dementia.

The following tests were carried out on the subjects (study and control) in a relaxed state and privacy was given utmost importance: Rye's auditory verbal learning test (AVLT), verbal fluency test (VFT) and working digit span test (WDST) to assess short-term memory, visual reproduction test (VRT), and validation span test (VST) were used to assess working memory.[2,5]

Statistical analysis was performed using SPSS software version 21. Initially, data were tested for normality using Kolmogorov-Smirnov test and Shapirowik Test. Since the data do not follow normal distribution, nonparametric tests were used which include Mann–Whitney *U*-test and correlation-regression analysis was performed using Spearman rank correlation.

RESULTS

AVLT

Mean, standard deviation (SD), Median, interquartile range (IQR) of the AVLT test for diabetic patients and normal subjects are shown in Table 1. The median scores of the test are depicted in Figure 1 and Table 1 also shows *P* values of the same using Mann–Whitney *U*-test. The memory scores (%) in the diabetic patients were found to be decreased, and the decrease in the scores was statistically significant when compared to normal subjects ($P < 0.001$).

VFT

Mean, SD, Median, IQR of the VFT test for diabetic patients and normal subjects are shown in Table 1. The median scores of the test are depicted in Figure 1 and Table 1 also shows *P* values of the same using Mann–Whitney *U*-test. The memory scores (%) in the diabetic patients were found to be decreased, and the decrease in the scores was statistically significant when compared to normal subjects ($P < 0.001$).

VRT

Mean, SD, Median, IQR of the VRT test for diabetic patients and normal subjects are shown in Table 1. The median scores of the test are depicted in Figure 1 and Table 1 also shows *P* values of the same using Mann–Whitney *U*-test. The memory scores (%) in the diabetic patients were found to be decreased, and the decrease in the scores was statistically significant when compared to normal subjects ($P < 0.001$).

WDST

Mean, SD, Median, IQR of the WDST test for diabetic patients and normal subjects are shown in Table 1. The median scores of the test are depicted in Figure 1 and Table 1 also shows *P* values of the same using Mann–Whitney *U*-test. The memory scores (%) in the diabetic patients were found to be decreased, and the decrease in the scores was statistically significant when compared to normal subjects ($P < 0.001$).

VST

Total score (%), mean, SD, Median, IQR of the VST test for diabetic patients and normal subjects are shown in Table 1. The median scores of the test are depicted in Figure 1 and

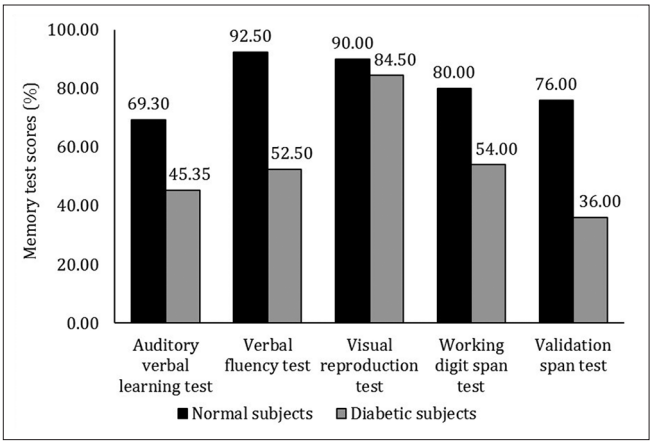

Figure 1: Memory status: Normal subjects vs Diabetic subjects

Table 1: Memory tests of normal subjects and diabetic patients

Tests	Diabetic subjects			Normal subjects			*P* value
	Mean±SD	MED	IQR	Mean±SD	MED	IQR	
AVLT	45.23±12.85	45.35	18.4	69.24±9.33	69.3	14.6	<0.001 (S)
VFT	52.95±16.07	52.5	19.4	90.10±9.23	92.5	17.5	<0.001 (S)
VRT	81.22±16.02	84.5	13	90.4±6.59	90	11	<0.001 (S)
WDST	56.84±18.19	54	24	81.04±13.47	80	22	<0.001 (S)
VST	34.7±16.45	36	20	75.96±14.33	76	24	<0.001 (S)

S: Significant, SD: Standard deviation, AVLT: Auditory verbal learning test, VFT: Verbal fluency test, VRT: Visual reproduction test, WDST: Working digit span test, VST: Validation span test, IQR: Interquartile range

Table 1 also shows *P* values of the same using Mann–Whitney *U*-test. The memory scores (%) in the diabetic patients were found to be decreased, and the decrease in the scores was statistically significant when compared to normal subjects ($P < 0.0001$).

*All five tests scores were decreased and found to be statistically significant ($P < 0.001$) in diabetic patients when compared to normal subjects.

DISCUSSION

This study was conducted in the McGann Hospital, Shivamogga. The protocol was explained to all those who volunteered for the study, and informed consent was obtained.

Median of memory scores found in normal subjects was as follows: AVLT: 69.3, VFT: 92.5, VRT: 90, WDST: 80, and VST: 75. Median of memory scores found in diabetes patients were as follows: AVLT: 45.35, VFT: 52.5, VRT: 84.5, WDST: 54, and VST: 36.

Okereke et al. did community-level study of which 553 men and 405 women had DM showed men with DM had significantly greater 2 years cognitive decline than men without DM, and longer duration of DM was associated with worse decline (*P*-trends < or = 0.01), and women with DM had significantly greater 4 years cognitive decline in all outcomes than women without DM. In women, as in men, there was generally greater cognitive decline with longer duration of DM.[6]

Ruis et al. did study on 183 diabetic patients (61.2% males) and 69 control subjects (47.8% males) showed age was inversely related with performance on tasks for memory and information-processing speed in diabetic patients and showed sex was significantly related to cognitive performance. Patients with recent screen-detected type 2 diabetes performed significantly worse on memory functions, in particular, the immediate memory compared with control subjects.[7]

Alka et al. conducted 4 years prospective study on 999 white men and women aged 42-89 years according to their blood glucose levels, applied three tests, *viz.*; Mini-mental state examination, VFT and trial marking *B*-test and concluded that women with DM had 4 fold increased risk of a major cognitive decline on the VFT when compared with women without diabetes.[8]

In a study done by Solanki et al. "Neurocognitive impairment and comorbid depression in patients of DM" on diabetes patients ($n = 50$) and normal subjects ($n = 30$) found that 48% of elderly diabetic patients showed cognitive impairment.[9]

Nandipati et al. in their study "Cognition in nondemented diabetic older adults" on 314 diabetic patients and normal subjects showed that cognitive functioning was significantly lower in diabetic subjects compared to nondiabetics with $P = 0.01$.[10]

In the present study, all five memory tests scores were significantly decreased in diabetic patients ($P < 0.001$) when compared to normal subjects. The decrease in the scores in diabetes patients was may be due to hyperglycemia,[11] vascular disease,[12] hypoglycemia,[12] insulin resistance,[13] and amyloid deposition.[14] Changes in glutamate receptor subtypes, in second messenger systems, and in protein kinases may account for alter in synaptic plasticity in addition to cerebrovascular changes, oxidative stress, non-enzymatic protein glycation, insulin and alterations in neuronal calcium homeostasis.[11] Type 2 diabetes has been associated with decrease in psychomotor speed, frontal lobe executive function, verbal memory, processing speed, working memory, immediate recall, visual retention, and attention.[15] Furthermore, some of the factors combine and produce additive effect to produce cognitive decline like type of diabetes, comorbidities, age of onset, duration of diabetes and type of therapy.[16]

Limitations

Prospective studies are required to examine the putative link between noninsulin dependent diabetes and cognitive dysfunction, because only by using such study designs can a causal relationship be established. Since different studies have utilized different psychological tests, there is a need to develop a standard study design that can be employed in testing cognitive impairment in type 2 diabetes.

CONCLUSION

This study shows that the short term and working memory scores were decreased in diabetic patients, and this decrease in memory status was statistically significant when compared to age and gender-matched normal subjects. The main hypothesis to explain the decline in memory status in diabetic patients with respect to duration, gender, age, blood sugar levels, and glycemic control are hyperglycemia, hypoglycemia, microvascular injury, insulin resistance, or hyperinsulinemia. The relationship is worth investigating further because both diabetes and dementia are becoming major public health threats in view of the continuous aging of the population. A better understanding of the mechanisms linking diabetes to cognition may uncover new possibilities for prevention of age-related cognitive decline.

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