Study of working and short-term memory status in patients of type 1 diabetes mellitus as compared to healthy individuals

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<u>Abstract</u>

Background: Diabetes mellitus causes cognitive dysfunction, slows psychomotor responses all of which may affect short term and working memory. Study was conducted to see the effect of Diabetes mellitus on cognitive function mostly on short term and working memory. Aim: To study working and short term memory status in diabetic patients for early detection of neuropathic changes. Objectives: 1. To determine working and short term memory status in type 1 diabetics and in age and sex matched healthy controls. 2. To compare and correlate above tests in patients of type 1 diabetes mellitus with age and sex matched healthy controls. Material and Methods: The present study was conducted in civil hospital, Latur, Maharashtra. The study group consisted of 60 cases of diagnosed type 1 diabetes mellitus who were taking regular treatment in age group of 18-25 yrs and 60 age and sex matched nondiabetic healthy individuals. Working and short term memory status was determined by different tests like mini mental state examination, working digit span test – forward, working digit span test – backward, Letter / number sequencing test, Test of ten words. Results: Statistical analysis done by using unpaired t-test revealed significant decline in performance on short term and working memory tests in type 1 diabetics as compared to healthy individuals(p<0.01).

Key Words: Diabetes mellitus, Short term memory, Working memory, Cognitive dysfunction.

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INTRODUCTION

Diabetes mellitus is a state of chronic hyperglycaemia, classically associated with symptoms of excessive thirst and increased urine volume¹. It can be defined as a state of diminished insulin action due to its decreased availability or effectiveness in varying combinations1.Memory is one of the most important cognitive domains with respect to everyday function and is the process of storing, encoding and retrieving information. Short-term memory refers to the function that temporarily retains stimuli that have just been perceived. Through repetition, information may be transferred from short-term memory to long-term memory. Working memory is a form of short-term memory that keeps information available, usually for very short periods, while the individual plans action based on it². It is used for thinking about what is already known and for deriving conclusions on the basis of that knowledge; therefore, working memory is fundamental to successful completion of many activities. Individuals with type I diabetes mellitus show cognitive dysfunction characterized by slowing of mental speed and diminished mental flexibility³.Cognition have correlated with P300 wave in many studies⁴. A growing number of studies have shown that diabetes is associated with impaired cognitive processes⁵. In cases with questionable dementia, DM is

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associated with a faster rate of cognitive decline (measured by Mini-Mental State Examination), while such an association is questionable in individuals without dementia⁶. Hence it is important to examine short–term memory and working memory in type 1 diabetics to see the adverse effects of diabetes on cognitive performance and help in early intervention of the disease

MATERIAL AND METHODS

The study was conducted on 120 individuals aged 18-25 yrs of which 60 were cases of type 1 diabetes mellitus of either sex who were taking treatment regularly and 60 were age and sex matched nondiabetic healthy individuals. The subjects included were non-smokers, non-alcoholics, non-hypertensive. They were not suffering from any psychiatric disorders affecting their psychomotor abilities.

Study protocol:

The study was approved by institutional ethical committee. A written informed consent was taken from every individual prior to conduction of the study. The detail history was taken, general and systemic examination of each subject was carried out. The objectives and detailed procedure were explained to each individual before performing the tests.

Short term and working memory status were examined by following tests:

- 1. Mini mental state examination
- 2. Working digit span test forward
- 3. Working digit span test backward
- 4. Letter / number sequencing
- 5. Test of ten words
- 1. Mini mental state examination: The minimental state examination (MMSE) is a brief 30point questionnaire test that is used for screening of cognitive impairment. It examines functions including arithmetic, memory and orientation. The MMSE test includes simple questions and problems in a number of areas: the time and place of the test, repeating lists of words, arithmetic such as the serial sevens, language use and comprehension, and basic motor skills.

The number of points assigned per category is usually consistent:

Category	Possible points	Description			
Orientation to time	5	From broadest to most narrow. Orientation to time has been correlated with future decline			
Orientation to place	5	From broadest to most narrow. This is sometimes narrowed down to streets and sometimes to			
		floor.			
Registration	3	Repeating named prompts			
Attention and calculation	5	Serial sevensor spelling "world" backwards. It has been suggested that serial sevens may be more			
		appropriate in a population where English is not the first language.			
Recall	3	Registration recall			
Language	2	Naming a pencil and a watch			
Repetition	1	Speaking back a phrase			
Complex commands	6	Varies. Can involve drawing figure shown.			

- 2. Working digit span test- forward: In this digit span test, a series of lists of numbers was presented verbally to the subject. The standard Wechsler Memory Scales Digit Span Test was modified for this experiment to test working memory more fully. Here each number was uttered to the subject at the rate of one word per second. Then subjects were asked to recall the numbers in ascending numerical order (forward). For example, for the sequence 2-6-1-5-3, the correct response for working digit span forwards 1-2-3-5-6. The test score is the number of lists that are remembered correctly⁷.
- **3.** Working digit span test-backward: In this digit span test, a series of lists of numbers was presented verbally to the subject at the rate of one word per second. The subjects were asked to recall the numbers in descending numerical order (backward). For example, for the sequence 2-6-1-5-3, the correct response for working digit span backward is 6-5-3-2-1. The test score is the number of lists that are remembered correctly⁷.
- 4. Letter number sequencing test :In the Letter/Number Sequencing Test from the Wechsler Memory Scales, a series of lists of numbers mixed with letters was presented verbally. The subject must recall the list, stating the numbers in ascending numerical order followed by the letters in alphabetical order. For example, for the sequence 2-D-6-A-1-G, the correct response is 1-2-6 A-D-G. The test score is the number of lists that are remembered correctly⁷.
- 5. Test of ten words: In this test a list of ten words was presented verbally to the subject at the rate of one word per second. The subject is given the instructions to repeat each word slowly after the examiner says the word. Then the subject was asked to recall the words he could remember. The test score is the number of words remembered correctly.

STATISTICAL ANALYSIS

Statistical analysis was done using unpaired t-test with the use of Software IBM SPSS(Version 21.0). p value <0.05 was considered as significant

RESULTS

Table 1: Comparison of mean values of Mini mental state examination(MMSE) in controls and type 1 diabetics							
Parameter	Group	Mean± SD	t Value	P Value	S/NS		
Mini Mental State Examination	I : Control	27.53 ±1.09					
	ll: Type I DM	19.63 ±1.97	27.17	<0.001	S		

Table no. 1 shows statistically significant difference between the mean scores of Mini Mental State Examination among group I and group II subjects. (P value < 0.001) by unpaired t-test.

Table 2: Comparison of mean va	lues of	[•] Working o	ligit span 1	testin contro	ls and	type 1 diabetics
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Parameter	Group	Mean± SD	t Value	P Value	S/NS
Working Digit	I : Control	9.26 ±1.33			
span test (F)	II: Type I DM	5.90 ±1.24	14.31	< 0.001	S
Working Digit	I : Control	9.31 ±1.58			
span test (B)	II: Type I DM	5.80 ±1.21	13.66	< 0.001	S
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Table no. 2 : By applying unpaired t-test, a statistically significant difference was noted between mean scores of Working Digit span test among group I and group II subjects (P value < 0.001).

Tak	ole 3: Comparison of mean valu	es of Letter Num	ber Sequencing	testin conti	rols and typ	e 1 diabet	ics
	Parameter	Group	Mean± SD	t Value	P Value	S/NS	
		I : Control	20.30 ±1.79				
	Letter Number sequencing	II: Type I DM	9.51 ±1.56	35.20	< 0.001	S	

Table no. 3 :A statistically significant difference was found between the mean scores of Letter Number Sequencing among group I and group II subjects (P value < 0.001) by unpaired t-test.

Table 4: Comparison of mean values of Test of ten words in controls and type 1 diabetics								
Parameter	Group	Mean± SD	t Value	P Value	S/NS			
Test of ten words	I : Control II: Type I DM	7.25± 1.243 4.43±1.07	13.250	<0.001	S			

Table no. 4 : A statistically significant difference was found between the mean scores of Test of ten words among group I and group II subjects (P value < 0.001) by unpaired t-test.

DISCUSSION

The results suggested a significant decrease in scores of mini mental state examination, working digit span test:forward and backward, letter number sequencing test, test of ten words in type I diabetics as compared to normal. Thus, there was a significant decline in performance on short term and working memory tests in patients of type I diabetes mellitus as compared to healthy individuals. Our results are supported by similar findings in the studies conducted by Mirena Valkova, Boyko Staminov et al⁸, R.K. Solanki, Vaibhav Dubey et al⁹. In the brain, the medial temporal lobe and in particular hippocampus are the principle structures involved with memory performance¹⁰. Functional MRI studies have shown that prefrontal brain activity is associated with the performance of tasks very similar to those performed in working memory tests¹¹.The decreased performance in type I diabetic may be due to hypoglycaemia. Hypoglycaemia is the most common side effect seen in

insulin treated Ι diabetic patients¹². type Neuropathological observations have indicated that the brain is susceptible to neuroglycopenia in a rostro-caudal direction, while the cerebral cortex and hippocampus being most sensitive and the brainstem and spinal cord being most resistant¹³. In the brain, glucose is transported across the cell membranes by facilitated diffusion, mediated by the glucose transport proteins GLUT1 and GLUT314. These are localized in the membranes of brain endothelial cells, astrocytes, and neurones. In diabetes, there is disturbance in the interaction between local energy demands of the brain and the regional distribution of GLUT1 andGLUT3 receptors. In animals, working memory tasks have been shown to exert high demands on brain extracellular glucose¹⁵.All these changes lead to decreased memory performance in patients of type I diabetes mellitus.

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