

## Comparison of Long-Term Memory Function in Elderly across Mind Activity and Diabetes Mellitus-Type 2

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### Abstract

**Objectives:** While Diabetes Mellitus (DM) affects cognitive functions and the Long Term Memory (LTM), several different strategies are designed to control harmful consequences of DM. This study is investigating whether having Mind Activity (MA) can make any difference in LTM function of individuals with DM.

**Design:** The participants (n=80) were classified in 4 groups based on having DM or not and having MA or not. Methods: The LTM and MA were assessed respectively by the word-list of Tulving and Pearlstone, and a self-report form. The BG concentrations were measured in vitro.

**Results:** The results showed a significant negative correlation between BG concentrations and LTM scores in group with DM. The LTM function is significantly lower in group with DM and no-Mind Activity (nMA) respectively than the group with no-Diabetes Mellitus (nDM) and with MA. Also the LTM scores of the groups with nDM&MA, nDM&MA, DM&MA, nDM&MA, nDM&nMA and nDM&MA which were respectively higher than those of the groups with nDM&nMA, DM&MA, DM&nMA, DM&nMA, DM&nMA and DM&MA were statistically significant.

**Conclusions:** The weaker BG control in patients with DM, the higher LTM dysfunction; and LTM function is in close relationship with DM (negatively) and MA (positively). Patients with DM and individuals with nDM who have their minds active in elderly, may less likely confront LTM dysfunction than matched groups who do not have active minds.

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## Introduction

Human bodies' cells need oxygen and fuel to survive. It is clear that gastrointestinal tract which provides fuel is sometimes empty. Thus, there should be a storage to reserve the nutrition materials for future consumption when the stomach is vacant. Liver cells transform glucose to glycogen and save it. This mission is possible in presence of insulin hormone, which is a peptide made by Pancreas glands. Therefore, when glucose and insulin are both present in bloodstream, part of the glucose would be consumed as fuel and the other part would be reserved as glycogen (1).

Diabetes Mellitus (DM), which is characterized with increased blood sugar over a long period, is due to either the pancreas not producing enough insulin (type 1) or the cells of the body not responding properly to the produced insulin (type 2). In advanced stages of DM type 2, exhausted  $\beta$  cells of pancreas gradually decrease releasing insulin (2). Continued uncontrolled high density of Blood Glucose (BG) leads to initiate abnormal activities and altered structure of blood vessels of various tissues in all over body (3). This, in turn, leads to the elevated risk of heart attacks and cardiovascular diseases (4), stroke (5), advanced kidney diseases (6), retinopathy and blindness (7), ischemia (8) peripheral organs gangrene (9), peripheral neuropathy (10), autonomic nervous system dysfunctions (11), delirium (12), and microstructural abnormalities in brain white matter (13).

Neuropathy in diabetic individuals averagely initiates in 10 to 20 years after DM onset (14; 2). Thus, psychophysiological aspects (15; 16) of DM are important consequences. One of these considering outcomes is cognitive impairment. Type 2 DM has effects on cognitive functions (17; 16; 14; 18) autobiographical memory (19) and slowing down psychomotor system overall (20). Likewise, Elias and colleagues (21) could find chronic DM affecting cognitive performance only when men and women were combined for analyses.

Beside numerous medical treatments, lifestyle is proven to be effective in reducing diabetic symptoms through the Finnish Diabetes Prevention Study (22) and the Diabetes Prevention Program (23). Dietary modification that targeted a low-calorie, high fiber diet and moderate intensity physical activity resulted in a moderate weight loss. In both studies, the risk reduction for diabetes was 58% at 4 years (24). In other trials, overweight Japanese men (aged 30 to 60 years) with impaired fasting glucose were randomized to either a frequent intervention group or a control group for 36 months. Results showed an incidence of type 2 diabetes of 12.2% in the frequent intervention group and 16.6% in the control group, with an adjusted Hazard Ratio in the frequent intervention group of 0.56 (25). A 20 year follow up trial showed that risk of diabetes incident and vision-threatening retinopathy was reduced by 47%. (26). A group-based lifestyle interventions over 6 years could prevent or delay diabetes for up to 14 years after the active intervention and also led to reduced cardiovascular diseases (27).

In addition to medical benefits of life style alteration, educating Diabetes Self-Management Strategies (DSMS) has been suggested by health experts since couple of years ago (28) as a systematic intervention that involves active patient participation in self-monitoring (physiological processes) and /or decision making/managing (29). Continuing DSMS education and supports, through several standards (30) can help the individuals, even children and adolescents (31), to overcome barriers and to cope with the ongoing demands in order to facilitate changes during the course of treatment and life transitions (32). Furthermore, DSMS recognizes that patient-provider collaboration and the enablement of problem-solving skills are crucial to the individual's ability for sustained self-care (33). As the literature have shown DSMS education is recognized successful in assuaging various elements which are involved in DM (34; 35; 36; 37).

Moreover, advanced age per se is considered as a risk factor for type 2 DM (38; 39) since, the disposal of glucose load is progressively impaired during aging (40). Furthermore, literature have shown that elderly is associated with different kinds of cognitive dysfunctions (41); and as were shown earlier, DM can influence cognitive functions as well. Hence, elderlies with DM are at risk of cognitive dysfunctions much more than nDM or younger individuals are. However, studies have revealed that even in old age the neuroplasticity of the human brain enables it to rewire, readapt, renew and not only change its structure but also generate new neuron connections (42). As an evidence for cognitive improvement, a meta-analysis study has shown that mind-body exercise, Tai Chi, positively affective on memory functions, spatially verbal working memory in elderlies (43), since, physical exercise may be an important tool for managing cognitive health in advanced age as well (44). Also research have applied particularly computer-based training (45) with the objective to improve the mental cognition of elderly (46; 47; 48).

To put it briefly, despite all the promising interventions which have been designed and investigated until now, the gap for reinforcing and rehabilitating the cognitive abilities of patients with DM is not still considered appropriately. Thus, this study is going to investigate if MA and BG are correlated with LTM functions among Iranian elderly samples of type 2 DM.

## Methods

### Participants

All participants were selected from referrals to a Clinical Laboratory in Iran. The volunteers were matched for age (50 to 65 years old,  $M = 56.4$  and  $SD = 3.85$ ), type 2 DM duration (had been diagnosed as type 2 DM by an endocrinologist for 10 to 20 years) and education (they all had college diploma or bachelor degree). Due to effect of intelligence on memory (49), education level is considered as an indicator of intelligence which was

not accessible to measure before DM onset. The participants were classified in four groups (20 per each groups) based on having MA or not and having DM or not, as the following: the group with "no Diabetes Mellitus" & "Mind Activity" (nDM&MA), the group with "no Diabetes Mellitus" & "no Mind Activity" (nDM&nMA), the group with "Diabetes Mellitus" & "Mind Active" (DM&MA) and the group with "Diabetes Mellitus" & "no Mind Activity" (DM&nMA).

In order to keep the conditions matched for all groups, the subjects of all groups were excluded if they had been labeled as any disease but pre-hypertension (120/80mm Hg to 139/89mm Hg) and/or high blood lipid (Cholesterol: 200 to 300mg/ml, Triglyceride: 150 to 250mg/ml). Since, hematophobia leads to anxiety and anxiety in turn elevates blood sugar (50), all participants were controlled for hematophobia by reporting any sign of exposure arousal.

### Measures

#### *Blood Glucose:*

Blood samples were collected in sterilized tubes and the serums were separated by centrifuging. Fasting BG levels were measured by glucose- oxidase method (51) using Pars Azmun's kit for Blood Glucose (Pars Azmun Company, Iran).

#### *Long-Term Memory:*

To assess this variable the word-list of Tulving and Pearlstone (52), which was initially designed to evaluate the impact of clue word on recalling all items of a cluster, was used. Remembering every item gains a single score, thus participants could receive a score between 0 and 48 from the whole list.

#### *Mind Activity:*

The participants of mind active groups reported having mind activities such as reading, writing, memorizing, playing chess, solving cross-words or Sudoku averagely 2 hours per day as part of their life style; or having active mind-demanding jobs such as

teaching, reading, writing, memorizing, categorizing, organizing, managing, designing, planning, problem solving and calculating.

### Procedure

Subjects were asked to listen carefully to examiner when she was reading the words to them, since they had to remember the words after about 60 minutes [this interval was necessary for synaptic consolidation to form (53)]. During the interval between two stages of listening and remembering, blood samples were collected and the examiner talked to participants about irrelevant subjects in order to prevent them thinking or repeating the words. After 60 minutes, subject were asked to remember and say out the words of every word class when the clue words were presented.

Statistical analyses were performed using Statistical Package for the Social Sciences (SPSS, version 19).

### Results

Mean and (standard deviation) on fasting BG concentrations of all groups of nDM&MA, nDM&nMA, DM&MA and DM&nMA are respectively 82.20 (7.04), 83.75 (7.00), 158.45 (42.93), and 162.30 (43.20). Mean and (standard deviation) on LTM scores of all groups with nDM&MA, nDM&nMA, DM&MA and DM&nMA are respectively 36.40 (4.83), 24.90 (4.67), 30.6 (5.51), and 18.55 (4.17).

### BG and LTM in subjects with DM

Through Pearson's Correlation Coefficient, a significant negative correlation was found between BG concentrations and LTM scores ( $r = - .39$ ,  $df = 39$ ,  $p < .05$ ) of subjects with DM.

### Comparing LTM Between groups with DM&nDM, MA&nMA

Table 1 shows that the results for mean difference of LTM between subjects with DM and nDM was significant ( $P < .001$ ), and also the mean difference of two subjects with MA and nMA was statistically significant ( $P < .0001$ ).

**Table 1.** Independent t-test to compare LTM between groups

Groups with	Df	Mean differences	Sig.
DM-nDM	78	6.075	0.001
MA-nMA	78	11.775	0.0001

Abbreviations: Diabetes Mellitus (DM), no Diabetes Mellitus (nDM), Mind Activity (MA), no Mind Activity (nMA), Long Term Memory (LTM).

### Comparing groups on LTM

All pair-groups (nDM&MA with nDM&nMA, nDM&nMA with DM&MA, DM&MA with DM&nMA, DM&nMA with nDM&MA, nDM&nMA with DM&nMA, and nDM&MA with DM&MA) were compared on LTM scores by one-way ANOVA which was statistically significant [ $F = 50.38$ ,  $df = 3-76$ ,  $P < .0001$ ]. Tukey test was used as the post hoc test and the results are reported in table 2.

As it is shown in the table 2, the LTM scores in the group with nDM&MA were significantly higher than those of the subjects of nDM&nMA. The individuals with DM&MA achieved higher scores in the LTM than individuals with nDM&nMA did and the patients with DM&MA gained higher scores for the LTM than individuals with DM&nMA did. The subjects with DM&nMA scored significantly lower than the group with nDM&MA did on LTM function. Also the higher scores of group with nDM&nMA on LTM function than those of participants with DM&nMA were statistically significant. The last comparison indicated that the individuals with nDM&MA can score significantly higher than the individuals with DM&MA on LTM scores.

**Table 2.** Tukey test to compare LTM between groups

Groups with	Mean differences	Sig.
nDM&MA and nDM&nMA	11.5	0.0001
nDM&nMA and DM&MA	5.7	0.002
DM&MA and DM&nMA	12.05	0.0001
nDM&MA and DM&nMA	17.85	0.0001
nDM&nMA and DM&nMA	6.35	0.0001

P < .0016, due to Bonferroni correction in P value, significant level was divided into number of comparison groups (n=6).  
*Abbreviations:* no Diabetes Mellitus & Mind Activity (nDM&MA), no Diabetes Mellitus & no Mind Activity (nDM&nMA), Diabetes Mellitus & Mind Activity (DM&MA), Diabetes Mellitus & no Mind Activity (DM&nMA), Long Term Memory (LTM)

## Discussion

This study aimed to investigate the relationship of LTM function and BG concentrations in individuals with DM type 2 and found the correlation negatively meaningful. Also the LTM difference between the subjects with DM and nDM was considered, which indicated that LTM function is stronger in nDM individuals in comparison to individuals with DM. Moreover, the LTM function between individuals with MA and nMA was considered and found stronger in groups with MA than those with nMA. The mean differences between LTM function of all groups of nDM&MA with nDM&nMA, nDM&nMA with DM&MA, DM&MA with DM&nMA, DM&nMA with nDM&MA, nDM&nMA with DM&nMA, and nDM&MA with DM&MA were statistically significant indicating that the LTM of individuals with nDM&MA operates better in comparison with the LTM individuals with nDM&nMA, DM&nMA and DM&MA; and the LTM function in the group with DM-nMA is weaker than both groups with nDM-nMA and DM-MA. The most important and challenging finding of this study is stronger LTM of individuals with DM-MA in comparison to the participants with nDM-nMA.

Present study's findings showed that there is a negative association between level of BG and LTM function in type 2 DM, which means that LTM function declines as BG levels increase in patients with DM which had been left almost uninvestigated. Thus, this finding alerts investigators and physicians about DM disease: the higher uncontrolled BG concentrations, the weaker LTM function.

Also, current study found that comparing the groups with DM and nDM on LTM was meaningful, which means that LTM performs better in individuals with nDM than individuals with DM. Moreover, LTM of individuals with nDM&MA operated better in comparison with LTM of individuals with DM&MA. Also the group with nDM&nMA scores was better than those of individuals with DM&nMA. These results are representing the DM-induced harmful consequences in the cognitive functions domain. Similar to the findings of Coker & Shumaker (17), Elias and colleagues (21), Ho et al. (16), Leung & Bryant (19), McNay et al. (14) and Wataria et al. (18), this study demonstrated that individuals with DM suffer from more cognitive dysfunctions in comparison to people with nDM. Briefly, weaker performance of the groups with DM on LTM function, reveals that considera-



ble DM- induced long term memory dysfunction, prioritize the people with DM for rehabilitation and prevention programs, especially when DM is synchronized with advanced age.

The LTM was compared between individuals with MA and nMA to see if MA is associated with memory function. Since the results found the group with MA performing highly better in LTM than the group with nMA, it can be concluded that high levels of MA in elderly is expected to be accompanied with better functions in LTM. This is compatible with the results of previous studies (46; 45; 47; 48; 43) who found MA associated with better function in cognitive and memory tasks in correlational and interventional models. Furthermore, these results are matched with better function of individuals with nDM&MA than people with nDM&nMA on LTM which is considered in current study. In addition, in comparing of subjects with DM&MA with individuals with DM&nMA on LTM function, a similar pattern was dominated. Therefore, when two groups are being compared, regardless of having DM or not, the MA side performs better on LTM tasks than nMA side.

LTM function in nDM&MA subjects was much better than that of DM&nMA participants. This finding is compatible with previous studies about DM impairments on cognitive function (17; 16; 19; 14; 18) and MA on LTM (46; 45; 47; 48; 43). Since people with DM&nMA are shown to be associated with two different sources of cognitive impairments (Diabetes Mellitus and mind inactivity) at the same time, they can be assumed to be more irritable to any kind of cognitive dysfunction.

The most challenging finding of the current study is that subjects with DM&MA showed stronger LTM than the group with nDM&nMA. It may be inferred that the relationship between LTM and MA is stronger than that of LTM with DM. This means that MA may soothe the harmful effects of DM. While these findings are promising, due to the method of this study, it is not possible to attribute better LTM functions to MA. Hence,

the results lead us to conclude that keeping minds active in elderly is highly beneficial for individuals with DM and also individuals with nDM, since it is associated with better LTM function.

It is acknowledged that the frequent excluding criteria of this study may have reduced the study's sample size. Also, the researchers did not have access to intelligence level of subjects with DM before DM onset to control intelligence effects on LTM appropriately. In addition, the whole mechanism of memory includes interaction of several parts and types of memory, while this study investigated single type of LTM. The investigator are also aware of limited interval time between "word reading to subjects" and "asking them to recall the words" which was not unavoidable due to the time limitation of subjects. Moreover, this study was designed as a correlation and could not reveal the possible moderator role of MA for DM- induced LTM dysfunction. These points limit the present study that can be addressed in future studies.

In conclusion, the weaker BG control in patients with DM, the higher LTM dysfunction; and LTM function is in close relationship with DM (negatively) and MA (positively). Patients with DM and nDM individuals who have their minds active in elderly, may less likely confront LTM dysfunction than matched groups who do not have active minds. It means, MA as a DSMS is positively associated with LTM function in patients with DM who are at risk of cognitive dysfunctions.

### Declaration of Conflicting Interests

"None Declared".

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