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RESEARCH ARTICLE

A study of cognitive assessment in Type 2 diabetes mellitus patients

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ABSTRACT

Background: Studying the deleterious effects of Type 2 diabetes mellitus (T2DM) on cognition is gaining a lot of attention. Cognition is measured by the P300 component of event-related potentials (ERPs). Hence, we studied P300 in T2DM. **Aims and Objectives:** This study was done with the objective to evaluate cognition of T2DM and also to evaluate factors associated with impaired cognition. **Materials and Methods:** Thirty T2DM and 30 controls matched for their age and gender were selected considering inclusion and exclusion criteria. Cognitive assessment was done using mini-mental state examination, and subjects with scores higher than 25 (maximum score = 30) were included in the study. After ruling out hearing loss by pure tone audiometry, P300 recording was done on them using RMS EMG EP MARK II machine. The resulting data were statistically analyzed. **Results:** P300 latencies ($P < 0.001$**) were longer in T2DM when compared with nondiabetics. P300 latencies showed significant positive correlation ($r = 0.390$*; $P = 0.033$) with T2DM duration. A significant difference was found in P300 latency between diabetic hypertensives ($P = 0.003$) and diabetic nonhypertensive, among diabetics with dyslipidemia ($P = 0.047$) and diabetics without dyslipidemia and between diabetic smokers ($P < 0.001$) and diabetic non-smokers. **Conclusion:** Cognitive function of T2DM subjects should be examined on a regular basis using ERPs because there could be an association between T2DM duration and cognitive deterioration. T2DM, along with dyslipidemia, hypertension, and smoking, further aggravates the possibility of cognitive dysfunction. We conclude that dementia can be diagnosed by ERP P300 in the initial phase.

KEY WORDS: Event-related Potential; P300 Latency; Cognition; Type 2 Diabetes Mellitus; Mini-mental State Examination; Dementia

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a disease that leads to deleterious complications, including cognitive impairment.[1-4] The detrimental effects of T2DM on eyes, kidney, cardiovascular, and peripheral nervous systems are very well known. Not much is studied on cognitive impairment in T2DM. The performance of T2DM subjects on various cognitive domains is reduced.

Cognitive dysfunction directly affects the quality of life, and they become dependent. It may ultimately be a huge concern to elder T2DM subjects much similar to the usual complications of blood vessels.[5]

T2DM is usually associated with hypertension and dyslipidemia. Recent studies show enough proof suggesting the association of cognition with these comorbidities.[6,7]

Mini-mental state examination (MMSE) is one of the neuropsychological tests most commonly used as a screening

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tool.[8,9] Age and education level plays a key role in the MMSE scores.[10]

MMSE may not detect minute cognitive deficits which may be present in T2DM subjects. Earlier studies have concluded that MMSE has decreased repeatability as well as a reduced sensitivity and specificity.[9]

Event-related potentials (ERPs) show the pace of the cognitive process and are an electrophysiological index of the relative timing of the process of stimulus estimation and cognitive impairment in recent years.[11,12]

P300 was included in our study to detect cognitive deterioration in T2DM with normal MMSE scores. This study aimed to assess P300 latency in diabetics to test cognition and compare it with that of age- and sex-matched controls. Furthermore, it aimed to correlate P300 latency with duration of diabetes and to study the association of P300 latency with the coexisting conditions of diabetes such as hypertension, dyslipidemia, and smoking in diabetics.

MATERIALS AND METHODS

A total of 30 T2DM subjects were included in the study group, who had more than 2 years duration of T2DM (22 males and 8 females; mean age: 62.26 ± 7.98 years) attending the diabetic clinic and medical Outpatient Department in the RL Jalappa Hospital, Kolar, and 30 non-diabetic subjects matched for their gender and age were included in the control group [Table 1]. The control group was recruited from Sri Devaraj Urs Medical College (SDUMC) campus and RL Jalappa Hospital. The ethical clearance from the institution was taken for the study. The selected subjects gave their informed consent.

T2DM subjects with chronic complications were excluded from the study group. T2DM subjects using medications such as sedatives, antidepressives, or neuroleptics or presenting with a history of meningitis, encephalitis, Alzheimer's diseases, blindness, stroke, and psychiatric disorder were excluded from the study.

Both the groups were instructed not to oil the scalp. They were also told to shampoo and dry their hair. The skin was prepared by scraping and cleaning. P300 cognitive evoked potential was recorded using RMS EMG EP MARK 2 machine in all the subjects. A silent room was chosen for the test. The individual was made to sit comfortably on a chair and was instructed to remain alert and count the rare stimulus presented unsystematically to the repeated stimulus (oddball paradigm).

Ag/Agcl disc electrodes were affixed with electrode gel with the reference electrode placed at Cz vertex scalp site, two active electrodes placed at mastoid processes (A1–A2). These active electrodes are linked. The ground electrode was placed at the forehead. Good lighting was maintained in the laboratory, and the impedance of the electrode was kept below 5 kΩ. The EMG RMS MARK II machine averaged and analyzed the evoked responses. The peak P300 latency [Figure 1] recordings and T2DM duration were correlated.

Statistical Analysis

SPSS 20.0 was the statistical software used to analyze data. Microsoft Word and Excel were used to generate tables. P300 recording was compared between T2DM and age and gender matched controls using independent *t*-test. To study the relationship between P300 latency and duration of T2DM, Pearson correlation was done. In the study group, to compare mean P300 values of T2DM between subjects with hypertension and those without hypertension, those with dyslipidemia, and those without dyslipidemia and also between smokers and non-smokers, independent *t*-test was used. The outcome of this statistical treatment helped us to draw conclusions.

RESULTS

In the present study, 60 subjects were selected. The study group comprised 30 T2DM (22 males and 8 females), aged 62.26 ± 7.98 years and with T2DM duration of 7.43 ± 4.15 years. The percentage of hypertensives was 43.33% and 30% in T2DM and non-diabetic group, respectively.

Table 1: Characteristics of the subjects

Subjects	Diabetics	Controls
Total (*n*)	30	30
Female *n* (%)	8 (26.66)	8 (26.66)
Male *n* (%)	22 (73.33)	22 (73.33)
Age (Mean±SD) (years)	62.26±7.98	62.6±8.01
Duration of T2DM (Mean±SD) (years)	7.43±4.15	-
Hypertension (%)	43.33	30
Dyslipidemia (%)	26.66	23.33
Smokers (%)	40	13.33

SD: Standard deviation, T2DM: Type 2 diabetes mellitus

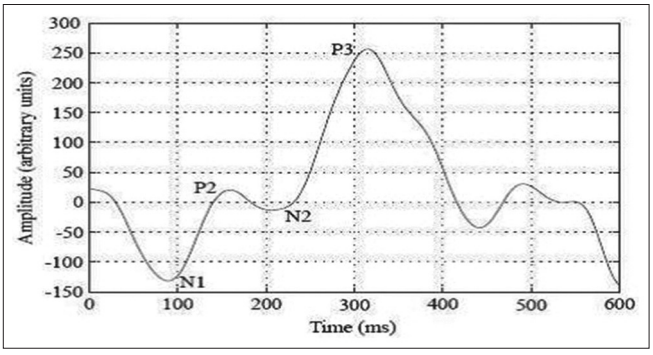

Figure 1: Normal P300 waveform

The percentage of dyslipidemia was 26.66% and 23.33% in T2DM and non-diabetic group, respectively. The percentage of smokers was 40% and 13.33% in T2DM and non-diabetic group, respectively [Table 1].

The mean MMSE scores between T2DM and control groups showed no statistical significance ($P = 0.924$). The difference in mean P300 latency values between T2DM and non-diabetic groups was significant statistically ($P < 0.001$**) [Table 2].

Figure 2 showed significant positive correlation ($r = 0.390$*; $P = 0.033$) between latency of P300 and T2DM duration. The difference in mean P300 latency values between diabetic hypertensives and diabetic nonhypertensives was significant ($P = 0.003$*) [Table 3].

Table 4 showed that the difference in mean P300 latency values between diabetics with dyslipidemia and diabetics without dyslipidemia was significant ($P = 0.047$*). There was a significant difference in mean P300 latency values between diabetic smokers and diabetic non-smokers ($P < 0.001$**) [Table 5].

DISCUSSION

In our study, the MMSE scores between T2DM and controls showed no significant difference. T2DM subjects showed significantly higher ($P < 0.001$**) latencies of ERP P300 than controls. There was significant positive correlation ($r = 0.390$*; $P = 0.033$) between P300 latencies and T2DM duration. A significant difference ($P = 0.003$*) was found in P300 latency between diabetic hypertensives and diabetic nonhypertensive and also between diabetics with dyslipidemia and diabetics without dyslipidemia ($P = 0.047$*). The difference in P300 latency was significant between diabetic smokers and diabetic non-smokers ($P < 0.001$**).

MMSE was used as a screening tool to measure cognition in all subjects. Subjects whose MMSE score was more than 25 were chosen. A score of <25 indicates cognitive dysfunction.

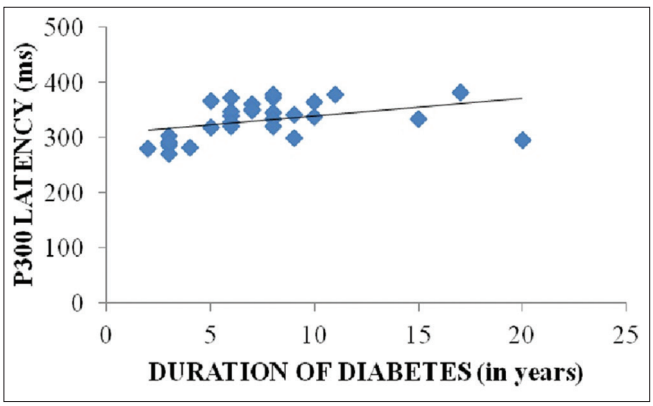

Figure 2: Correlation of P300 latency (ms) with the duration of diabetes mellitus

The MMSE scores between T2DM and controls in our study were comparable showing no signs of cognitive dysfunction.

Among all objective cognitive tests, P300 ERP is considered to be a very receptive tool for studying cognition in T2DM. The pace of neural events involved in short-term memory and attention is provided by P300 ERP.[13] In the present study, P300 latencies were significantly higher in T2DM subjects than controls which are in accordance with other studies.[13-17] The probable cause for prolonged P300 wave could be chronic sustained hyperglycemia. Hyperglycemia damages the neurons in the brain by oxidative stress-mediated free radical formation, augmented release of inflammatory cytokines and glycosylation process without the action of enzymes. Furthermore, persistent hyperglycemia reduces neural growth in the hippocampus, which hampers the working memory and learning and thereby leading to a degeneration of hippocampus and cell death. Functional magnetic resonance imaging in the quiescent state revealed decreased functional connections of hippocampus bilaterally to extensive regions in T2DM when compared to healthy controls.[11]

Table 2: MMSE scores and P300 latency values (ms) of diabetics and controls

Variables	Diabetics (30) (Mean±SD)	Controls (30) (Mean±SD)	*P*-value
MMSE score	26.30±1.44	26.26±1.22	0.924
P300 Latency (ms)	331.53±33.63	295.27±27.74	0.001**

*Significant (0.05), MMSE: Mini-mental state examination, SD: Standard deviation

Table 3: Association between P300 latency (ms) and hypertension in diabetics

Diabetics	Number of subjects	P300 latency (ms) (Mean±SD)	*P*-value
Hypertensives	13	350.32±20.03	0.003*
Nonhypertensives	17	317.15±35.25	

*Significant (0.05). SD: Standard deviation

Table 4: Association between P300 latency (ms) and dyslipidemia in diabetics

Diabetics	Number of subjects	P300 latency (ms) (Mean±SD)	*P*-value
Dyslipidemia	8	346.61±17.07	0.047*
No dyslipidemia	22	326.04±36.70	

*Significant (0.05). SD: Standard deviation

Table 5: Association between P300 latency (ms) and smoking in diabetics

Diabetics	Number of subjects	P300 latency (ms) (Mean±SD)	*P*-value
Smokers	12	360.94±16.85	0.001**
Non-smokers	18	311.92±26.99	

*Significant (0.05). SD: Standard deviation

A positive correlation was significant between P300 latencies and T2DM duration. This suggests that subjects with longer duration of T2DM had longer P300 latencies. Electrophysiological P300 test revealed that ailment period of T2DM is associated significantly with P300 latencies.[13,14] These conclusions suggest that T2DM duration is important in the cognitive impairment pathogenesis. The distorted function of brain and cognitive impairment could be as a result of an imbalance in metabolic processes and other factors. Long duration T2DM further augments atherosclerosis leading to stroke, resulting in the macrovascular disease of brain and brain infarctions and thereby cognitive deterioration.[13]

In our study, significant difference was found in P300 latency between diabetic hypertensives and diabetic nonhypertensive and also between diabetics with dyslipidemia and diabetics without dyslipidemia. T2DM usually does not occur isolated. Hypertension and T2DM, when combined together, augment the development of cognitive deterioration.[18-20] A similar study also concluded increased association of hypertension with T2DM group than the control group, and the difference in P300 was significant with the concurrence of T2DM and hypertension than the only T2DM.[13]

Cognitive decline due to hypertension is as a result of a load of blood pressure on the cerebral circulation, both on large and small vessels. Increased atherosclerosis is responsible for large vessel disease, whereas small vessel disease is unremitting because of remodeling of large and small arteries, impaired endothelial function and destruction of cerebral blood flow autoregulation leading to decrease in perfusion. All these results in ischemic or hemorrhagic stroke-causing necrosis in brain and cognitive deterioration.[13]

In the present study, the difference in P300 latency was significant between diabetic smokers and diabetic non-smokers. The study showed significantly longer latency in diabetic smokers, which may elucidate the effect of tobacco smoking and nicotine on cognition, as concluded in other studies.[21-23]

Strength and Limitationsof the Study

Two screening tools, MMSE and P300 were used to detect cognitive impairment in T2DM. Cognitive changes were revealed by P300 ERPs, which was not revealed by MMSE. The effect of comorbidities of T2DM such as hypertension and dyslipidemia was studied, and the effect of smoking on P300 was also studied.

The limitation of the study is that the glycemic status of T2DM was not included in the study. Hence, P300 latency between controlled and uncontrolled T2DM could not be studied. The gender variation on P300 in T2DM was also not studied.

CONCLUSION

The conclusions of our study support the hypothesis that there is an association between T2DM and impairment of cognition. Cognitive deterioration is very likely to develop in T2DM with an increase in the duration of the disease. P300 is a sensitive tool that can be used for uncovering early cognitive impairment in T2DM in whom MMSE has failed to detect. Thus, P300 may reveal cognitive decline at a very early stage in T2DM. The presence of coexisting conditions such as hypertension, dyslipidemia, and smoking in T2DM appears to aggravate cognitive impairment in a very significant way.

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