

## RESEARCH ARTICLE

# Does gender influence P300 latency and Mini Mental State Examination score in Type 2 Diabetes Mellitus patients?

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## ABSTRACT

**Background:** P300 event-related potentials (ERPs) is an electrophysiologic marker of cognitive ability which closely reflects cognitive functions. Type 2 Diabetes mellitus (T2DM) causes many complications. Diabetes mellitus-induced damage to the central nervous system is a key focus of research. Latest Magnetic resonance imaging evidence suggested that the changes in anatomy of brain is more rapidly seen in males than in females. This study was carried out to study the gender variations in P300 latency and Mini Mental State Examination (MMSE). **Aim and Objective:** To study the influence of gender on MMSE score as well as P300 ERP. **Materials and Methods:** 30 diagnosed Type 2 Diabetics aged above 40 years, with more than 2 years duration of diabetes were included in this study. MMSE questionnaire was administered to each diabetic and P300 was recorded using RMS EMG EP MARK 2 machine in all the diabetics. **Results:** The P300 ERP of male diabetics was prolonged significantly with mean  $\pm$  standard deviation (SD) of  $(347.01 \pm 31.55)$  whereas female diabetics had a mean  $\pm$  SD of  $(318.26 \pm 28.22; P = 0.014)$  and no significant difference was found between the mean MMSE scores of male diabetics  $(26.06 \pm 1.38)$  and female diabetics  $(26.13 \pm 1.30)$ . **Conclusion:** The change in P300 ERP is swifter in males when compared with females in the middle to old age. Compared to MMSE, P300 Latency is a sensitive electrophysiological tool for diagnosing early cognitive deterioration in T2DM.


**KEY WORDS:** Event-related Potentials; Gender; Cognitive Deterioration; Type 2 Diabetes Mellitus; Mini Mental State Examination

## INTRODUCTION

Diabetes mellitus is a hyperglycaemic state resulting in formation of Advanced glycation end-products which degenerates the neural machinery, myelin sheath and glial cells leading to deterioration in cognition of diabetics as well as prediabetics.<sup>[1]</sup>

magnetic resonance imaging measurement of anatomy of human brain including cerebral cortex shows reduction in volume size of gray matter of cerebral cortex as the person ages. In adults, there may be association of gender with varying degree of alteration of anatomic structures of brain. More rapid reduction of temporal and frontal lobes is seen in males than in females. Not much is known about influence of gender on measuring neurophysiological processing.<sup>[2]</sup>

P300 event-related potentials (ERP) is indicative of changes inside the brain during development and aging. Polich revealed in a Metaanalysis that ERP is suggestive of cognitive aging.<sup>[2]</sup> The ERPs are produced in the brain in reaction to a particular stimuli in the form of undersized voltages. The ERPs represent the cumulative sum of post-synaptic

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potentials which are generated by the synchronous firing of the large number of similarly oriented cortical pyramidal neurons during information processing.<sup>[3]</sup>

P300 in EEG is a positive deflection at about 300–600 ms subsequent to a rare stimuli with the maximum peak around 300 ms.<sup>[2,4]</sup> It probably points out at the neural activity pace or efficiency of information processing<sup>[5]</sup>

Mini Mental State Examination (MMSE) is a tool used to measure mental status systematically. The MMSE is an effective screening tool to measure cognition in older, community dwelling, hospitalized adults.<sup>[6]</sup>

The influence of gender on P300 potentials is less studied. This study was carried out to know the effect of gender on P300 potentials and MMSE scores in Type 2 diabetics.

## MATERIALS AND METHODS

30 Type 2 diabetics (15 males and 15 females) attending medicine Outpatient Department in the RL Jalappa Hospital, Kolar with more than 2 years duration of Type 2 Diabetes Mellitus (T2DM) were included in the study. Informed consent was obtained from these subjects. The ethical clearance for the study was obtained from the institution.

Diabetics with chronic complications were excluded from the study. Diabetics on antidepressives, or neuroleptics, sedatives or diabetics with a history of encephalitis, meningitis, Alzheimer's diseases, stroke, blindness and psychiatric disorder were excluded from the study.

The subjects were briefed not to apply oil to the scalp. They were further instructed to wash and dry their hair. The subjects were made to comfortably sit on a chair in a sound proof room. RMS EMG EP MARK 2 machine was used to record P300 ERP in all the subjects after ruling out hearing loss. Pure Tone Audiometry was used to rule out hearing loss. The skin preparation was done by scraping and cleaning. Electrodes were placed at four sites to record P300 potentials. Ag/AgCl disc electrodes were placed using 10-20 conduction paste 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. This is based on International 10–20 system. The impedance of the electrode was ensured to be less than 5 k $\Omega$ . If impedance was higher, cleaning of electrode site was repeated.

The subjects were instructed to alertly count the infrequent stimulus presented randomly to the frequent stimulus (oddball paradigm). The RMS EMG MARK II machine averaged and analyzed the evoked responses.

MMSE is a questionnaire consisting of 19 questions testing five areas of cognitive function: orientation, registration, attention and calculation, language and recall. 30 is the maximum score.

## Statistical Analysis

SPSS 20 was the statistical software used for analyzing data. P300 recording and MMSE score was compared between T2DM males and T2DM females using independent *t*-test.

## RESULTS

In this study, MMSE scores and P300 latency were obtained from 15 male diabetics and 15 female diabetics. Table 1 showed MMSE scores of diabetic males and females. The average mean  $\pm$  standard deviation (SD) MMSE score was  $26.06 \pm 1.38$  in Diabetic males and  $26.13 \pm 1.30$  in Diabetic females which showed no statistical difference with  $P = 0.893$ . Table 2 showed the P300 latency values of diabetic males and females. The difference in mean P300 latency values was statistically significant ( $P = 0.014^*$ ).

## DISCUSSION

In this study, there was significant prolongation of P300 latency in male diabetics with mean  $\pm$  SD of ( $347.01 \pm 31.55$ ) as compared to female diabetics ( $318.26 \pm 28.22$ ) with  $P = 0.014$  and no significant difference was found between the mean MMSE scores of male diabetics ( $26.06 \pm 1.38$ ) and female diabetics ( $26.13 \pm 1.30$ ).

Findings of this study imply that P300 latency is different in diabetic males and females. This could probably be because of variations in some of the volumes of neural regions, size and numbers of neural cells and the actions of various neurotransmitters influences the ERP.<sup>[2]</sup> Variations

**Table 1: MMSE scores of diabetic males and females**

Groups	Number of subjects	Mean MMSE score	Std. deviation	P-value
Diabetic males	15	26.06	1.38	0.893
Diabetic females	15	26.13	1.30	

**Table 2: P300 latency values (ms) of diabetic males and females**

Groups	Number of subjects	Mean P300 latency (ms)	Std. deviation	P value
Diabetic males	15	347.01	31.55	0.014*
Diabetic females	15	318.26	28.22	

\*significant at the 0.05 level

in P300 because of gender is due to differences in strategies of processing, anatomical differences like larger corpus callosum in females, variations in maturity rates of neurons and asymmetry of cerebral hemisphere in females and males.<sup>[7]</sup>

ERP recordings during global-local reaction time task to compare asymmetry in hemisphere and processing biases in adult men and women revealed a quicker response of women to local targets than men. Women also had greater P300 responses following local stimuli. This study concluded that differences in performances in females and males arise from biological variations in hemispheric asymmetry.<sup>[8]</sup>

Additionally, MR imaging showed that reduction in volumes of frontal as well as temporal areas with age were more in males than in females. These anatomical changes are reflected in the P300 latency, as it indicates more hasty brain change in males.<sup>[2]</sup> This may be the reason for prolonged P300 latency in males.

Few other studies have concluded that prolongation of ERP with aging may start much earlier in females and much later in males. However, not much is known about this earlier, prolonged P300 latency in females. This may be related to deficiency of estrogen in postmenopausal women. Firstly, experimental evidence indicates that conjugated estrogen acts as a growth factor on cholinergic neurons. Secondly, as cholinergic neurons of rodents and primate basal forebrain have estrogen and low affinity nerve growth factor receptors, estrogen acts collectively thereby regulating survival, differentiation, regeneration and plasticity of the neurons. Thirdly, the risk in elderly women of Alzheimer's dementia apparently decreases in postmenopausal women with estrogen replacement therapy with improvement in dementia test scores as well. These results are very important for women because of its preventive and therapeutic implications.<sup>[9]</sup>

As per research, DHEA, free testosterone are negatively correlated with P300 latency prolongation especially in older T2DM which is very vital in preventing and treating cognitive deterioration in both males and females.<sup>[10]</sup>

The present study didn't show significant difference in MMSE scores between diabetic males and females. A study by Braverman *et al.* has revealed that Electrophysiological test like P300 latency was more predictive of cognitive dysfunction than MMSE score and also that P300 could precisely recognize borderline/impaired memory.<sup>[11]</sup>

### Strength and Limitations of the Study

The effect of gender on P300 and MMSE score was studied. Not many studies are carried out in this regard.

It is difficult to detect early deterioration in cognition in diabetics owing to the "ceiling effect" in simple

neuropsychological tests, such as MMSE.<sup>[12]</sup> Additionally, the questionnaire is dependent on oral response and reading and writing. Therefore, performance will be poor in cognitively normal hearing and visually impaired subjects, intubated, have low English literacy, or those with other communication disorders.<sup>[6]</sup>

Sample size should have been a little more. HbA1c of T2DM was not studied. Hence, P300 latency between controlled and uncontrolled T2DM could not be studied.

### CONCLUSION

Males may experience more rapid change of P300 latency than females in middle to old age. Hyperglycaemia in Diabetes Mellitus further aggravates this change in P300 latency. Further research is required to determine whether these changes reflect neural pathophysiology, or is mediated by such factors as neuroanatomic differences, body temperature, or mild auditory deficits. Owing to the ceiling effect, MMSE does not provide adequate sensitivity in the detection of executive functions. Early deterioration in cognition in elderly diabetic patients can, however, be detected using complicated neuropsychological tests. When compared with standard neuropsychological tests, P300 a sensitive, objective electrophysiological method, can be used for detection of early deterioration in cognition in elderly diabetics. More studies need to be done in this area to test the consistency of the findings.

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