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Original Article

Auditory Late Latency Response in Individuals with Type 2 Diabetes Mellitus

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OBJECTIVES: The study was done to compare Auditory late latency response (ALLR) in normal-hearing individuals without diabetes mellitus and normal-hearing individuals with type 2 diabetes mellitus (T2DM).

MATERIALS and METHODS: A total of 50 participants within the age range of 40-60 years were enrolled in the study based on the inclusion and exclusion criteria. They were divided into two groups with one group consisting of 25 individuals with T2DM and the other group consisted of 25 individuals without diabetes as the control group.

RESULTS: The results revealed prolonged latencies and reduced amplitude of P1, N1 and P2 wave among individuals with T2DM compared to control group. There was a significant positive correlation observed for ALLR latency and duration of T2DM, and a negative correlation observed for ALLR amplitude and duration of T2DM.

CONCLUSION: The present study concluded that there is a problem in the encoding of speech at the cortical level despite normal hearing in individuals with type 2 diabetes mellitus.

KEYWORDS: Diabetes mellitus, latency, amplitude, auditory, duration

INTRODUCTION

Type 2 diabetes mellitus (T2DM) remains symptomless for a long time [1-4]. So, the inner ear dysfunctions in type 2 diabetes mellitus are noticeable only after the complications have developed. However, Bainbridge et al. [5] have indicated that if changes in hearing threshold and nerve function in individuals with diabetes are diagnosed early, it could offer valuable information for adopting control measures to monitor disease complications.

Auditory-evoked potentials are used to test the integrity of auditory system, and to make inferences about hearing. Many studies report either prolonged latencies or reduced amplitude of auditory brainstem response (ABR) and P300 in individuals with diabetic mellitus using tonal stimuli or click. Using speech-evoked ABR, it is reported that subcortical processing of speech is altered in individuals with diabetic mellitus [6]. However, there is lack of literature on the effect of diabetes on cortical level speech processing. Hence, the aim of this was to compare the auditory late latency response (ALLR) among individuals with T2DM and without diabetes using speech stimuli. The study also investigated the correlation between ALLR response and duration of T2DM. This study hypothesized that as compared to the individuals without T2DM, the individuals with T2DM would have longer latencies and less robust amplitudes for the speech-evoked ALLR.

MATERIALS and METHODS

A total of 25 participants were included in the T2DM group with equal gender representation, and age ranging from 40 to 60 years (mean age=52.16, SD=6.57). Another set of 25 participants was considered in the control group with age and gender matched individuals without diabetes. Ethical clearance was taken from the institutional ethical committee of Kasturba Medical College, Mangalore. Participants were informed about the purpose of the study, and an informed consent was obtained prior to their participation. Only individuals with bilateral pure tone thresholds within normal limits (<20 dB HL) at octave frequencies between 250 and 8000 Hz with bilateral 'A' type tympanogram having reflexes present in both ears participated in this study.

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All the participants had undergone routine speech audiometry test. All the T2DM participants had normal (>85%) speech identification score. The individuals in the T2DM group were diagnosed for a minimum of 1 year. The diagnosis of the T2DM participants have been done by endocrinologist based on the three tests: hemoglobin A1c, fasting plasma glucose test, and oral glucose tolerance. The average hemoglobin A1c testing showed 7.2% in the T2DM group, and 4.8% in the non-diabetic group. The average blood sugar level based on fasting plasma glucose level was 148.7 mg/dL in the T2DM group and 86.2 mg/dL in the non-diabetic group. The oral glucose tolerance level showed 210.3 mg/dL and 105.8 mg/dL in the T2DM and the non-diabetic group, respectively. These measurements were recorded three times, and an average value was considered for the diagnosis of diabetes. The T2DM group was under medication (glimepiride, glyburide, glipizide, and insulin). It was ascertained that no participant had presence of or history of hearing problem, vertigo, and neurologic or psychologic deficit. It was also ascertained that none had metabolic disorders.

"Intelligent Hearing System" version 3.92 was used to record speech-evoked ALLR. The speech stimulus used was a naturally produced consonant vowel (CV) /da/ spoken by a male talker. The stimulus was 232.54 ms long in duration with fundamental frequency of 192.493 Hz. Responses were recorded from electrode, with a contact impedance of <3 KΩ, positioned centrally on the vertex (non-inverting), right and left mastoid (inverting), and on the forehead (ground). Test stimuli were delivered monaurally through Etymotic ER-3 insert earphones at an intensity of 80 dBnHL with repetition rate of 0.5/s. A time window of 500 ms was used to record the responses, and the responses were obtained by averaging 300 stimulus sweeps. Participants were made to watch animated video on television with mute mode during ALLR recording. The acquired responses were amplified 50,000 times, and band pass filtered between 1 Hz and 30 Hz. ALLR was recorded from each ear, and was recorded two times to ascertain the reproducibility.

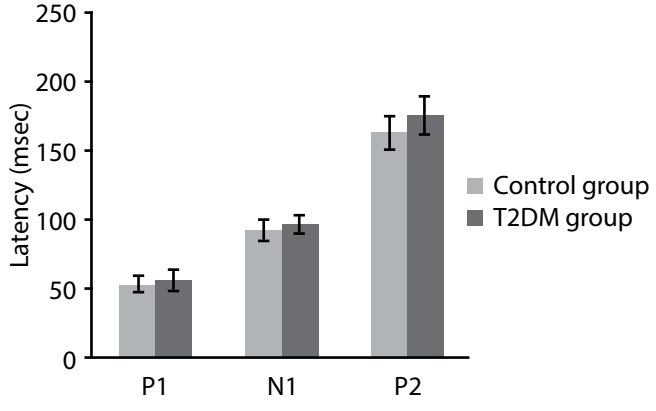

Figure 1. Mean and SD for latencies P1, N1, and P2 of speech-evoked ALLR in individuals with T2DM and the control group.

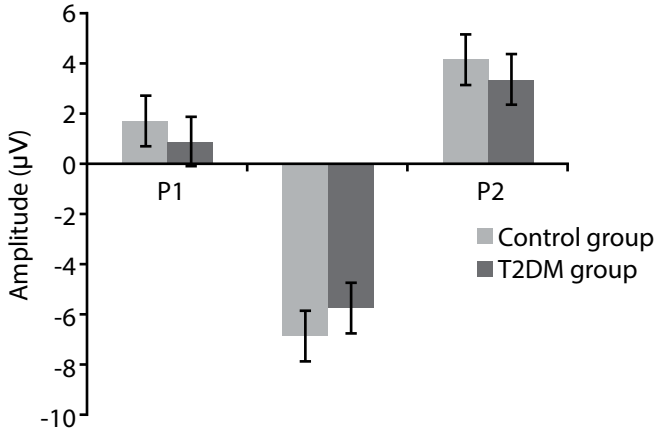

Figure 2. Mean and SD values for amplitude of P1, N1, and P2 in speech-evoked ALLR in the control group and the T2DM group.

Statistical Analysis

The latency and amplitude of wave components (P1, N1, and P2) of ALLR were analyzed offline. Statistical evaluations were carried out using The Statistical Packages for Social Sciences version 17 (IBM Corp; Armonk, NY, USA). Independent 't' test was implemented to evaluate the differences in latencies and amplitude in individuals with T2DM as compared to those in the control group. Pearson correlation analysis was performed to find the correlation between duration of diseases and ALLR waveform.

RESULTS

The latency and amplitude of the ALLR peak components P1, N1, and P2 were compared between the control group and the T2DM group. The mean and standard deviation obtained for the latency of P1 component was 53.28±5.98 (SD) ms in the control group, and 56.72±8.12 (SD) ms in the T2DM group. The results of independent 't' test revealed statistically significant difference in the mean latency of P1 in the T2DM group when compared to that in the control group [t (98)=2.41, p=0.018]. The mean latencies of N1 obtained for control group and the T2DM group were 93.32±7.67 (SD) ms and 97.48±7.43 (SD) ms, respectively. Comparison of the mean N1 latency showed statistically significant difference between the T2DM group and the control group [t(98)=2.75, p=0.007]. The mean P2 latency obtained for the control group was 163.64±12.50 (SD) ms, and for the T2DM group was 177.12±13.57(SD) ms. A significant difference was observed for P2 latency between the two groups [t (98)=5.16, p=0.00], indicating prolonged latencies in the T2DM group as compared to controls. The mean latency value of P1, N1, and P2 in the T2DM group and the control group is depicted in Figure 1.

The mean amplitude obtained for P1 in the control group was 1.68±0.84 (SD) μV, and in the T2DM group was 0.87±1.31 (SD) μV. A significant difference was observed in mean amplitude of P1 in the T2DM group as compared to that in the control group [t(98)=−3.69, p=0.00]. The mean amplitudes of N1 obtained for the control group and the T2DM group were -6.80±1.92 (SD) μV and −5.71±2.64 (SD) μV, respectively. Statistical analysis indicated that the N1 amplitude was significantly reduced in the T2DM group [t(98)=2.354, p=0.021] in comparison to that in the control group. The mean amplitude of P2 obtained in the control group was 4.09±1.54 (SD) μV, and reduction in the mean amplitude in the T2DM group was 3.30±1.32 (SD) μV. From the t value of independent t test, it can be inferred that there was significant difference [t(98)=−2.737, p=0.007] in P2 amplitude between the T2DM group and the control group. The mean and standard deviation of amplitude of P1, N1, and P2 in the T2DM group and the control group is shown in Figure 2.

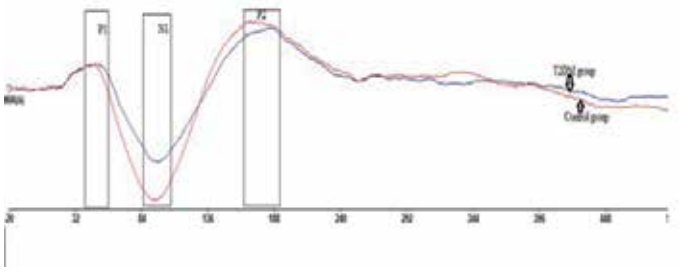

Figure 3. Grand average waveform of ALLR in the T2DM and the control groups. Blue solid line depicts the waveform obtained for T2DM, and red solid line depicts the waveform obtained for the control group.

The grand average waveform obtained for the T2DM group and the control group is shown in Figure 3. It indicates a shift in the latencies and decrement in amplitude in individuals with T2DM as compared to those in the control group.

Pearson product-moment correlation coefficient revealed significant positive correlation for the latencies of P1 (r=0.450, p=0.001), N1(r=0.591, p=0.000), and P2 (r=0.520, p=0.000). It indicates that with the progress in duration of T2DM, the peak latency of the ALLR increases. Result revealed significant negative correlation for the amplitude of P1(r=−0.579, p=0.000) and P2(r=−0.532, p=0.000). This indicates that amplitude decreases as duration of T2DM increases. And there was a positive correlation for N1(r=0.678, p=0.000) that indicates reduction in amplitude toward the positive side. Thus, it shows that as the duration of T2DM progresses, there is a reduction in the amplitude of P1, N1, and P2.

DISCUSSION

This showed that the mean latency of the ALLR peaks was prolonged in the T2DM group. Similarly, amplitude of ALLR peaks was observed to be reduced in the T2DM group as compared to that in the control group. The prolonged latency can be because of the delay in perceptual encoding of speech stimuli or conduction delay, and reduced amplitude may be due to reduction in the amount of firings in cortical level. Similar to the present research, there are other electrophysiological studies that indicate cortical dysfunction in individuals with diabetes mellitus. Andreadou et al. [7] reported increased latency of P300 and N200 in individuals with diabetes mellitus. The prolongation of N200 could be attributed to the deficit in attention and early stimulus processing, and for P300 it could be due to impairment in stimulus classification speed and working memory. No differences have been reported in latencies and amplitude of ALLR components N1 and P2, which may be because they were well trained in diabetes control, and attended clinic regularly. Moreover, the task used by them was oddball paradigm using two tones stimuli, but in this study, it was natural speech stimuli to evoke response. There are other studies reporting prolongation of P300 and N200 latency in diabetes mellitus as compared to that in the control group [7, 8]. They suggested that this prolongation in the latency is due to attention process, auditory discrimination, memory, semantic perspective, and poor glycemic control of these T2DM groups.

Similarly, there are evidences from the ABR studies supporting sub-cortical abnormalities in individuals with diabetes mellitus. Gupta et al. [6] reported prolonged latencies for onset (wave V) and frequency following response in speech-evoked ABR in individuals with T2DM, indicative of a conduction delay in sub-cortical level. Donald et al. [9] observed a significant delay in latencies I-III and I-V (interpeak latencies) of ABR in individuals with diabetes when compared to controls. The prolonged interpeak latencies may be due to central conduction delay from the brainstem to midbrain level in individuals with diabetes. Similarly, Gupta et al. [10] and Toth et al. [11] observed that latency of wave III and wave V was delayed, which was highly significant in individuals with T2DM. They concluded that this is indicative of neuropathy at brainstem and midbrain level. Studies also reported similar pattern of prolongation in the absolute latency of ABR and interpeak latencies. As both absolute as well as interpeak latencies are prolonged, studies suggest that T2DM affects peripheral as well central nervous system structures [12-14]. Latency values that are recorded in milliseconds indicate the neural travel time in response to auditory stimulation [15]. Huang et al. [16] had reported significantly prolonged interpeak latencies I-III and I-V, but there was no difference in interpeak latencies III-V. These findings suggest that there are chances of retro-cochlear dysfunction in the group with diabetes mellitus. The ABR studies indicate changes from auditory nerve to the subcortical level due to diabetes mellitus.

Moghaddam [17] had a contradictory observation with no significant difference in the ABR latencies in individuals with T2DM in comparison with those in the control group. He had opined the reason to be due to the experimental group having T2DM for duration of less than 10 years. They were also well trained in diabetes control, had good understanding about the medication, and attended clinic regularly.

In this study, there was significant reduction in the amplitude of P1, N1, and P2 wave components in individuals with T2DM as compared to controls. When the speech stimulus was presented, there was a decrease in the amplitude for each of the wave component. Similar amplitude reductions are observed in other electrophysiological studies. When changes in auditory brainstem response were assessed in individuals with diabetes, a prolonged latency reduction in amplitude was also observed. In diabetic group, the amplitudes of waves IV and V was reduced as compared to controls. There was an average reduction of 0.12 μV, which reflects the central conduction delay in diabetic group [9]. Similarly, it was found that there is a reduction in amplitude of ABR wave components I, III, and V in individuals with diabetes as compared with those with normal hearing [12]. A study had shown reduction in P300 amplitude in individuals with diabetes when compared to controls indicative of central auditory system dysfunction [7]. Gupta et al. [6] reported reduced amplitude for onset (wave V) and frequency following response for speech-evoked ABR in individuals with T2DM, which indicates that there is a reduction in number of firing at sub-cortical level. Thus, the reduction in amplitude can be attributed to any alteration in the auditory pathway due to T2DM.

Thus, this study revealed that in individuals with T2DM, as the duration of diabetes increases, ALLR latency increases and amplitude decreases. Hence, it can be postulated that as the duration of diabetes increases, degeneration of brain tissue progresses. This correlation may be due to diffuse degeneration of brain tissue, atrophy of dentate nucleus, cranial nerve demyelination, and angiopathy in individuals with long-term diabetes [18]. There are supporting electrophysiologic findings from individuals with long-term diabetes mellitus. Gupta et al. [10] found

that when duration of diabetes was 5-10 years, 7 out of 13 individuals (53.84%) showed delayed ABR response. And when the duration of diabetes increased (>10 years), 11 out of 12 individuals (91.66%) showed delayed ABR response. They concluded that the change in ABR response with progression of the disease is due to the emergence of central neuropathy. Similarly, it is proposed that duration of diabetes mellitus plays a major role in the development of associated central and peripheral neuropathies rather than degree of hyperglycemia and metabolic control [19]. The severity of cognitive decline and the duration of the diabetes mellitus are also related [20]. They also found a significant difference in the latency of P300 between the diabetes group with more than 5 years of disease and less than 5 years of disease. However, there were no linear correlation between the latency of P300 and duration of diabetes mellitus. They inferred that the signal conduction in the neural network is hampered by diabetes mellitus, which further deteriorated with increase in the duration of the disease.

CONCLUSION

This study showed prolongation in latencies and reduction in amplitude of ALLR in T2DM. There is also positive correlation with latencies and negative correlation with duration of disease. The prolonged latency and reduction in the amplitude of ALLR components in the absence of clinical signs indicate alteration in the cortical function in individuals with T2DM. These results can be helpful during the interpretation of cortical dysfunction in individuals with diabetes mellitus. This aspect should be considered while evaluating patients with T2DM in audiology clinics.

Ethics Committee Approval: Ethics committee approval was received for this study from Institutional ethical committee of Kasturba Medical College, Mangalore.

Informed Consent: Written informed consent was obtained from the participants who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – K.K.; Design – K.K., J.B.; Supervision - K.K., J.B.; Resource - K.K., J.B., A.V.; Materials - K.K., A.V.; Data Collection and/or Processing – A.V.; Analysis and/or Interpretation - K.K., A.V.; Literature Search – A.V.; Writing - K.K., J.B., A.V.; Critical Reviews – J.B.

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Conflict of Interest: The authors have no conflict of interest to declare.

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REFERENCES

1. Jorgensen MB. The inner ear in diabetes mellitus. Histological studies. Arch Otolaryngol 1961; 74: 373-81. [CrossRef]
2. Makishima K, Tanaka K. Pathological changes of the inner ear and central auditory pathway in diabetics. Ann Otol Rhinol Laryngol 1971; 80: 218-28. [CrossRef]
3. Maia CA, Campos CA. Diabetes mellitus as etiological factor of hearing loss. Braz J Otorhinolaryngol 2005; 71: 208-14. [CrossRef]
4. Alvarenga Kde F, Duarte JL, Silva DP, Agostinho-Pesse RS, Negrato CA, Costa OA. Cognitive P300 potential in subjects with Diabetes Mellitus. Braz J Otorhinolaryngol 2005; 71: 202-7. [CrossRef]
5. Bainbridge KE, Hoffman HJ, Cowie CC. Risk factors for hearing impairment among U.S. adults with diabetes: National Health and Nutrition Examination Survey 1999-2004. Diabetes Care 2011; 34: 1540-5. [CrossRef]
6. Gupta S, Bhat JS, Kumar K. Subcortical processing of speech in individuals with type 2 diabetes mellitus. Int J Diabetes Dev Ctries 2015; 35: 327-31. [CrossRef]
7. Andreadou E, Mitrakou A, Constantinides V, Triantafyllou N. Auditory P300 event-related potentials in patients with type 2 diabetes mellitus. J Diab Res Clin Met 2012; 1: 1. [CrossRef]
8. Tandon OP, Verma A, Ram BK. Cognitive dysfunction in NIDDM: P3 event related evoked potential study. Indian J Physiol Pharmacol 1999; 43: 383-8.
9. Donald MW, Bird CE, Lawson JS, Letemendia FJ, Monga TN, Surridge DH, et al. Delayed auditory brainstem responses in diabetes mellitus. J Neurol Neurosurg Psychiatry 1981; 44: 641-4. [CrossRef]
10. Gupta R, Aslam M, Hasan S, Siddiqi S. Type -2 diabetes mellitus and auditory brainstem responses a hospital based study. Indian J Endocrinol Metab 2010; 14: 9-11.
11. Tóth F, Várkonyi TT, Rovó L, Lengyel C, Légrády P, Jóri J, et al. Investigation of auditory brainstem function in diabetic patients. Int Tinnitus J 2003; 9: 84-6.
12. Abdulkadiroglu Z, Kaya A, Gonen S, Ilhan N. Brainstem auditory evoked potentials in patients with type 2 diabetes mellitus. Turk J Endocrinol Metab 1999; 1: 29-32.
13. Talebi M, Moosavi M, Mohamadzade NA, Mogadam R. Study on brainstem auditory evoked potentials in diabetes mellitus. Neurosciences (Riyadh) 2008; 13: 370-3.
14. Gupta S, Baweja P, Mittal S, Kumar A, Singh KD, Sharma R. Brainstem auditory evoked potential abnormalities in type 2 diabetes mellitus. N Am J Med Sci 2013; 5: 60. [CrossRef]
15. Näätänen R, Picton T. The N1 wave of the human electric and magnetic response to sound: a review and an analysis of the component structure. Psychophysiology 1987; 24: 375-425. [CrossRef]
16. Huang CR, Lu CH, Chang HW, Tsai NW, Chang WN. Brainstem auditory evoked potentials study in patients with diabetes mellitus. Acta Neurol Taiwan 2010; 19: 33-40.
17. Jabbari Moghaddam Y. Acoustic emissions from the inner ear and brain stem responses in type 2 diabetics. Int J Gen Med 2011; 4: 871-4. [CrossRef]
18. Reske-Nielsen E, Lundbæk K, Rafaelsen OJ. Pathological changes in the central and peripheral nervous system of young long-term diabetics : Diabetic encephalopathy. Diabetologia 1966; 1: 233-41. [CrossRef]
19. Dolu H, Ulas UH, Bolu E, Ozkardes A, Odabasi Z, Ozata M, et al. Evaluation of central neuropathy in type II diabetes mellitus by multimodal evoked potentials. Acta Neurol Belg 2003; 103: 206-11.
20. Hazari MAH, Reddy BR, Uzma N, Kumar BS. Cognitive impairment in type 2 diabetes mellitus. Int J Diabetes Mellit 2015; 3: 19-24. [CrossRef]