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RESEARCH ARTICLE

Gaps-in-noise test performance in subjects with type 2 diabetes mellitus

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Abstract

Background and Aim: Hearing loss is one of the complications of the type 2 diabetes mellitus, which commonly affects the central auditory processing. Gap in noise (GIN) test is an appropriate clinical tool for evaluating temporal auditory processing. The purpose of the present research was to compare the results of the GIN test in the diabetic patients with non-diabetic participants.

Methods: In this cross-sectional study, 30 subjects with type 2 diabetes (mean age=43.33, SD=4.7 years) and 30 normal hearing subjects (mean age=41.26, SD=6.2 years) were examined by the GIN test. The approximate GIN threshold and the percentage of correct answers were measured in all individuals.

Results: The findings showed an increase in the approximate GIN threshold and a decrease in the percentage of correct answers in the diabetic group in comparison with the non-diabetic group ($p<0.05$). In addition, the GIN threshold in the right ear was lower than the left one in the case group ($p<0.05$).

Conclusion: According to the derived results, the patients with type 2 diabetes mellitus appear to have defects in the temporal resolution domain the auditory stimuli and this disorder affects left ear more than right ear.

Keywords: Type 2 diabetes mellitus; gaps in noise test; central auditory processing; hearing loss

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Introduction

The diabetes mellitus refers to a group of metabolic disorders in common with hyperglycemia [1]. Estimates suggest that the prevalence rate of the type 2 diabetes in Iran will reach around 6.8% by 2025 [2], incurring significant costs to the healthcare system [2]. The diabetes-induced hyperglycemia through developing metabolic deficiencies of hydrocarbons and microangiopathy can cause a wide range of body disorders usually associated with the involvement of many tissues and organs, including muscles, kidneys and retina [3].

The auditory system, because of its high metabolic activity, is often the target organ for pathogenic effects of hyperglycemia [4,5]. The effect of diabetes on cochlear vascular units is known

as diabetic microangiopathy [6]. Systemic effects of microangiopathy have been confirmed in many studies [6,7]. The microangiopathy is associated with extensive damage to the endothelial tissue [6]. Such damages can be observed in various parts of the inner ear, including stria vascularis, basilar membrane and sensory hair cells [7]. Animal studies have shown condensation of marginal cells, swelling of intermediate cells and widening of the intercellular spaces in the stria vascularis in diabetic mice [8]. Human studies have also shown widespread damage to the inner ear, including the thickening of the stria vascularis, the thickening of the basilar membrane and the sclerosis of the auditory nerve [9], as well as a significant reduction in sensory hair cells [7].

There have been reports of progressive high-frequency sensorineural hearing loss (SNHL) in diabetic patients which can affect up to 93% of them [4]. In some studies, mid-frequency SNHL, unilateral hearing loss, and sudden hearing loss with or without symptoms of vestibular dysfunction have also been reported [3,10]. However, the pattern of hearing loss associated with diabetes is still not agreed by all researchers [11]. In a study, reduced distortion product otoacoustic emission (DPOAE) has been reported in these individuals, which mainly affects the right ear more than the left one, probably because the right ear advantage lost is accelerated by diabetes [12]. A review on auditory-evoked brainstem responses (ABR) has reported abnormalities such as the increase in wave V latency and the inter-peak latencies of I-V In type 2 diabetes population due to possible damage to the auditory nerve [13]. Research on diabetic patients has shown that the diabetes has more often central rather than peripheral effects on the neural conduction velocity of the human auditory nerve [13,14]. The prolonged latency of the wave V, without affecting the latency of the wave I, is evidence of a greater damage to the central auditory system (CNS) in the diabetic neuropathy [14].

The major CNS concern related to diabetes is the changes in the blood-brain barrier and metabolic functions [14]. Broad neurodegeneration occurs in the CNS during the disease due to the damage caused by increased free radicals and high rate of cell apoptosis and subsequent toxic effects produced by irregularities in the intracellular calcium [11]. Factors such as high blood pressure, the use of medications, and autonomic and peripheral neuropathies also affect brain function in diabetic patients [15]. Evidence suggests disturbances in the different brainstem area and the CNS of diabetic patients [5,7]. The research has confirmed the reduction in the number of ganglion cells in ventral and dorsal cochlear nuclei, superior olivary nucleus, inferior colliculus, and medial geniculate body in the diabetic patients [3].

The function of hearing is related to the factors that are more than mere recognition of the presence of an auditory signal, including neurophysiological and cognitive mechanisms that help decoding, perceiving, recognizing, and interpreting a signal leading by the CNS [16]. For this decoding to occur correctly, the acoustical cues of frequency, intensity, and timing must be processed [17]. The temporal auditory processing is an essential skill of the central auditory system. In fact, most dimensions of auditory information are affected by time [18]. The temporal auditory processing can be seen in a wide range from neurological timing in the auditory nerve to cortical processing for binaural hearing and speech perception [18]. Temporal resolution is one of the important aspects of temporal processing skills and may be defined as the ability of the auditory system to respond to rapid changes in the envelope of the auditory stimulus [19]. Central processing system abnormalities often cause disruption in normal speech perception and syllable recognition [19]. The tests developed for temporal processing are mainly based on the detection of the gaps between the stimulus segments [18]. The gap in noise (GIN) test is a good clinical tool for evaluating temporal processing ability [18]. This test was developed by Musiek et al. to assess the gap detection thresholds [20]. The sensitivity and specificity of this test for the lesions of the CNS have been determined previously [18].

Considering the possibility of CNS involvement

Table 1. Demographic characteristics of studied groups

			Diabetic group (n=30)	Control group (n=30)
Age (years) Mean (SD)			43.33 (4.7)	41.26 (6.2)
Gender (n, %)				
	Male		16 (53.33)	16 (53.33)
	Female		14 (46.66)	14 (46.66)
Acoustic reflex threshold (dB) Mean (SD)				
	Ipsilateral	Right	90.50 (6.34)	89.66 (6.42)
		Left	90.33 (6.14)	90.66 (5.20)
	Contralateral	Right	90.20 (7.39)	90.66 (6.39)
		Left	88.90 (5.74)	90.66 (5.68)
Pure tone average (dB) Mean (SD)		Right	11.00 (4.43)	11.00 (4.02)
		Left	12.50 (3.14)	11.00 (3.80)
TEOAE (screening mode)				
		Right	100% pass	100% pass
		Left	100% pass	100% pass
Tympanometry (type)				
		Right	100% An	100% An
		Left	100% An	100% An

TEOAE; transient evoked otoacoustic emissions

in the diabetic patients and due to limited studies about the GIN test in these patients, the present study aimed to investigate the ability to detect gap in noise in diabetic patients compared to non-diabetic subjects.

Methods

The present cross-sectional comparative study was conducted on 30 adults aged 25-50 years old (15 male and 15 female) with mean (SD) age of 43.33 (4.7) years diagnosed with the type 2 diabetes over at least 10 years and a medical record at the Diabetes Center of Bu Ali Hospital in Zahedan. They were selected among the 65 participating individuals aged 25-50 years old who did not have any exclusion criteria. The diabetes was diagnosed in these individuals based on the criteria set by the American Diabetes Association [21]. The protocol used in this study was approved by Zahedan University of Medical Science's Human Research Ethics Committee's Code No. 8199. All research participants signed the informed consent to participate in the study after explaining the details of the research. The control group consisted of 30 employees aged 25-50 years old with mean (SD) age 41.26 (6.2) years, (15 male and 15 female) from the staff of the Zahedan School of Rehabilitation by simple random sampling (Table 1). The participants in the study were all right-handed and monolingual. Exclusion criteria were kidney, ocular, cardiovascular and CNS-related diseases, hypertension, history of head trauma by a specialist physician based on imaging assessment, medical tests and clinical examination. Other exclusion criteria were use of ototoxic drugs, exposure to acoustic trauma, smoking, a family history of hearing loss, abnormalities in external auditory meatus and tympanic membrane, the absence of contralateral and ipsilateral stapedial reflexes, abnormal tympanogram and auditory thresholds more than

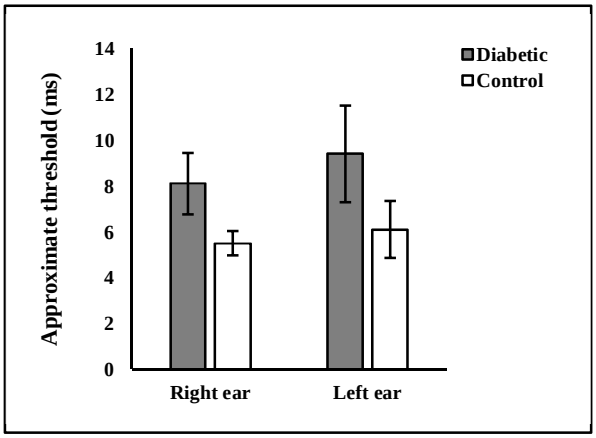

Fig. 1. Mean approximate threshold (milliseconds) in diabetic and control groups, *p<0.05.

15 dB HL at frequencies of 500-4000 Hz. Audiological evaluation were performed using a diagnostic audiometer (AC33, Interacoustic, Denmark) and tympanometer (Zodiac 901, GN Otometrics, Denmark) by an expert audiologist. In addition all the subjects had normal transient evoked otoacoustic emissions (TEOAE) (signal to noise ratio> +6 dB) results which had performed using an Echo lab system (Labat International, Italy) in screening mode.

All subjects were tested while seated in an acoustically controlled sound booth. The GIN stimuli, which were recorded on a compact disc, were played on a Samsung DVD-HD860 DVD/ CD player and passed through a calibrated AC33 Interacoustic diagnostic audiometer to TDH-39 matched earphones. The stimuli were presented at 50 dB SL according to pure tone average to each ear independently.

The test items consisted of a series of 6-sec segments of broadband noise containing 0 to 3 silent intervals or gaps per noise segment. The interstimulus interval between successive noise segments was 5 sec and the gap durations presented were 2, 3, 4, 5, 6, 8, 10, 12, 15, and 20 msec.

The test was performed on two headphones and started randomly in each patient with the right or left ear. The subjects were instructed to push the response button as they heard a gap. The approximate GIN threshold was calculated as the shortest gap perceived by the subject in at least four of the six presentations.

The combined percent correct answers across all gaps (the overall number of gaps detected per test list) were also calculated. This index was obtained from the sum of the correct answers minus the false positive responses divided by the total gaps in each list. Two false positives were negligible and, if there were more, the training of how to respond was repeated. The GIN detection test has four lists; in each list, each of the temporal gaps (2-3-4-5-6-8-10-12-15-20) has been presented six times randomly and 10 training items were also run before the test items. According to the previous research, two lists are sufficient to perform the test, so in this study two lists (selected at random from 4 original lists) were used to avoid fatigue and reduce test time [18].

In this study, Shapiro-Wilk test was used to evaluate the normality of data and Mann-Whitney U test to compare the means of approximate GIN thresholds and the combined percent correct answers between diabetic and non-diabetic groups with 95% confidence interval.

Results

In the present study, the approximate GIN threshold in the case group for the left and right ears was 9.4 (SD=2.10) ms and 8.1 (SD=1.33) ms, respectively, which were significantly different from the control group with the approximate GIN threshold of 6.1 (1.24) ms for left ear and 5.50 (0.52) ms for right ear ($p<0.001$ for both ears, Fig. 1). This difference between the two groups was also observed in the percentage of correct answer. The percentage of correct answer in the case group in the left and right ears were 48.30 (9.80) and 52.0 (9.01), respectively, which had a significant difference with the control group with the percentage of correct answer of 66.0 (5.50) for the left ear and 66.0 (4.16) for the right ear ($p<0.001$ for both ears, Fig. 2).

Comparison of approximate GIN threshold and the percentage of correct answers among the males and females of the control group showed no significant difference ($p>0.05$). In the case

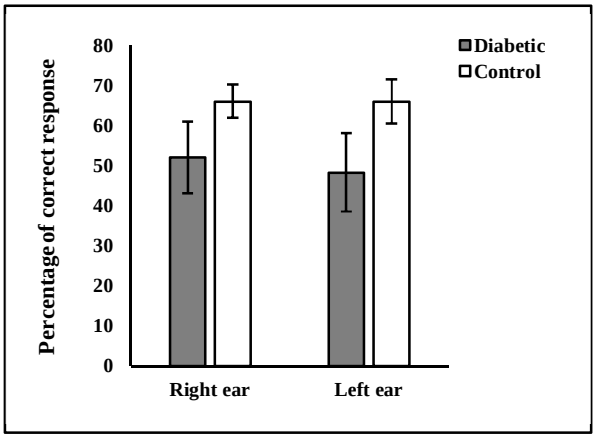

Fig. 2. Mean percentage of correct response in diabetic and control groups, *p<0.05.

group, although the females with diabetes had higher approximate GIN threshold (females=9.3 (1.50) ms, males=8.3 (1.90) ms), and lower percentage of correct answers (females=47.20 (9.40%,) males=52.3 (9.0%)), but this difference was not statistically significant (p>0.05). The mean approximate GIN threshold of detected GIN between the right and left ears was significant only in the case group (p<0.05) (Table 2). However, there was no significant difference between the percentage of correct answers of the right and left ears in both groups and the mean threshold in the control group.

Discussion

In the present study, the mean approximate GIN threshold and percentage of GIN correct answers were compared in diabetics and non-diabetic participants. The study results showed that the GIN test threshold in the left and right ears of diabetic people was 9.4 and 8.1 ms, respectively, and the percentage of correct answers was respectively 48.30 and 52.0%, indicating statistically significant difference with the non-diabetic group. In fact, the history of diabetes has increased the threshold and reduced the percentage of correct answers in the GIN test. Musiek et al. found that the mean approximate GIN threshold in the detection of gap in noise in patients with central auditory processing disorder (CAPD) in both ears was more than in their control group. They conclude that people with confirmed central auditory nervous system (CANS) involvement are weaker in the temporal resolution skill [20]. According to the results of the present study, it would be reasonable to conclude that the diabetic people maybe have some degree of CANS processing lesions but more studies are needed and all the confounding variable should be controlled. In particular, one of the inclusion criteria of patients for the study was the normal TEOAE and PTA. Previous studies have shown that the neurological dysfunction could have a disturbing effect on the temporal processing [20,22,23]. Removing the auditory cortex in humans and animals has a devastating effect on the temporal processing ability [24,25]. As the GIN test has relatively good sensitivity to CANS lesions [20], the weaker performance of diabetics in this study suggests that CANS, similar to the cochlea, is probably influenced by hyperglycemia. Chronic hyperglycemic condition results pathophysiological changes in the central nervous system [14].

Previous studies have shown that myelin tissue deficiency and other neuronal components and reduced dendritic branching are developed

Table 2. Mean (standard deviation) gap detection threshold percentages of correct responses in both ears of the diabetic and control groups

GIN parameters	Diabetic			Control		
	Left ear	Right ear	p	Left ear	Right ear	p
Threshold	9.40 (2.10)	8.10 (1.33)	0.02	6.13 (1.24)	5.53 (0.51)	0.34
Correct answer	48.26 (9.75)	51.60 (9.01)	0.28	65.80 (5.49)	67.80 (4.16)	0.43

GIN; gap in noise

significantly due to hyperglycemic damage in the peripheral nervous system [6]. Increasing the byproducts of glucose metabolism causes neuropathy in at least 50% of type 2 diabetics [4]. Animal studies have shown that mice with a high galactose diet have lower density of ganglionic neurons [8]. These histopathologic changes reduce the neural conduction velocity in diabetic patients [4]. Most studies examining diabetic people using auditory evoked potential (AEP), have reported prolonged latencies of the ABR waves especially for later wave components which can be delayed by three times more than the normal population [26,27]. This finding, similar to the results of the present study, shows the damage to the central auditory pathways. Reducing the neural conduction velocity at different levels of the CANS will have a detrimental effect on the processing velocity of auditory stimuli and it will probably increase the GIN threshold. Previous studies evaluating this test in patients with multiple sclerosis (MS) [22], CAPD [19], insular stroke [28] and neuropathy [9], similar to the finding of the present study, have shown weaken temporal resolution skill. Consequently, given the overlap of the results of these studies, it can be concluded that the diabetic people, like people with CAPD and MS, experience some degree of impairment in the central auditory processing. Evidence suggests the abnormalities in the CANS areas particularly in the upper part of the brainstem and in the central auditory areas of the diabetic patients [3]. Given the fact that these parts of the brain stem and the auditory cortex play an essential role in the encoding of the temporal features of auditory stimuli [19], people with diabetes are likely to have some degree of abnormalities in the upper part of the auditory system.

Comparison between ears showed there was an advantage of one ear over the other in terms of gap detection threshold. In some of the audiologic tests, such as speech in noise assessment, performance is expected to improve for the right ear due to left hemisphere advantage in performing the auditory tasks associated with temporal characteristics [17]. This pattern was observed in this study and the GIN detection threshold was lower in the right ear of diabetic subjects. Despite right ear advantage decay has been shown in diabetics, especially among the middle aged and older populations [12], but data from this study indicated that the right ear is still better in temporal auditory processing tasks. This is probably due to diabetes-induced neuronal damage [15] in the longer pathway of transmission of the left ear information to the dominant hemisphere (left cerebral hemisphere) in the processing of the temporal characteristic of auditory stimulus [17].

In the present study, GIN test results were not affected by gender which is consistent with the results from previous report [22]. There are also investigations have shown better performance of males in temporal processing of auditory stimuli [29,30]. Zaidan et al. observed slightly better responses by males than females in a gap detection task but the studied male group was musicians. Musicians have shown superior performance in temporal processing skills [31]. It seems likely that the difference in the results of this work with our study can be the heterogeneity of the studied groups in the study of Zaidan et al., in being familiar or not with music. In the study conducted by Amaral and Colella-Santos, the research tried to verify the performance of time processing ability in normal school children by using the GIN test in age range of 8 to 10 years. Their results showed no statistical differences among age groups or ears. The difference between the present study and their study seems the significant difference in age with our study group. Perhaps the maturity of temporal processing in males seems to be earlier than females [30]. To confirm or reject the impact of sex on this test in diabetic patients, further research is needed in homogeneous and heterogeneous of different ages and with various skills by controlling all the confounding and effective factors on this test. In this study, unfortunately, cognitive characteristics and mental health status did not considered precisely (although according to medical records and internal specialist visit the patients in this study do not have any central nervous system deficits). It is suggested that in the future

studies these factors be considered.

Conclusion

Evidence of the present study suggests a strong association between diabetes and central auditory processing problems. This could also consider auditory system among organs that should be examined periodically in these individuals and if needed, the person will be subject to hearing rehabilitation program.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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