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RESEARCH ARTICLE

Comparing the gap in noise test results in patients with type 1 diabetes and normal subjects

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Abstract

Background and Aim: Type 1 diabetes (T1D) is a common disorder that can cause various conflicts in the central nervous system (CNS). One of the important abilities of the CNS is the temporal processing. The purpose of this study was to compare the ability of temporal processing in patients with T1D and normal subjects using the gap in noise (GIN) test.

Methods: In this cross-sectional study, 25 T1D patients aged 20 to 30 years old and 25 normal subjects in the same age range were selected through available sampling method and were evaluated by gap in noise test. The level of HbA1c shows how the quality of metabolic control of diabetes has changed over the past 2 to 3 months. The relationship between the approximate threshold (ATh) values and the percent correct answers to the GIN test with HbA1c was investigated.

Results: Both ATh and percent correct responses were significantly different between patients with T1D and normal subjects in both ears and in both sexes ($p<0.05$). Moreover, the results showed a significant correlation between HbA1c with ATh and the percent correct responses. Also, there was no significant correlation between the duration of the disease with the ATh and the percent correct responses to GIN test.

Conclusion: Patients with TID have a weaker outcome than their normal counterparts during the GIN test. These results may indicate a defect in the ability to temporal processing in these subjects.

Keywords: Auditory temporal processing; type 1 diabetes; gap in noise test; approximate threshold; percent correct answers

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Introduction

Diabetes is metabolic disorder that has been associated with various pathological changes in the human body [1] It is also a chronic and progressive metabolic disorder, with its early symptoms occurring when the pancreas is not able to produce sufficient amounts of insulin or the body cannot properly and efficiently use the produced insulin [2]. Specifically, type 1 diabetes (T1D) is a chronic autoimmune disease that occurs as a result of destruction or damage to beta cells in the Langerhans, insulin

deficiency, and hyperglycemia or hyperglycemia [3]. Long-term infection with this disease can cause disturbances in the cranial nerves and peripheral nerves and organs such as eyes and ears [4]. Also, imaging studies showed a significant reduction in brain activity in the temporuroperitoneal portion during hypoglycemia. Considering the high dependence of the human brain on glucose as its main source of energy, it seems normal to be highly vulnerable to hypoglycemia. This means that hypoglycemia can disturb a significant degree of brain function [5]. Toxic effects of hyperglycemia are among other factors contributing to the changes and disturbances of the central nervous system (CNS) [6]. These changes can disturb the function of central auditory processing (CAP) and auditory temporal processing [5,7]. The importance of auditory temporal processing and its relation to speech perception has been proved in previous studies [8]. Clarity or temporal distinction is one of the aspects of auditory temporal processing, and is the shortest delay time a person can distinguish between two hearing impairments [9]. Auditory cortex and brainstem structures are commonly referred to as time distinction. Time distinction can be evaluated using a variety of methods. One of the few tests available for examining the time distinction is the gap in noise (GIN) test [10]. This test is also one of the few temporal processing evaluations that provides information on its sensitivity and specificity to central auditory nervous system waste. The sensitivity of this test is 72% and its specificity is 94%. The sensitivity of this test to cortical lesions seems to be greater than brain stem involvement [9]. Regarding the lack of time clarity studies in people with type 1 diabetes, the aim of this study was to compare the GIN test results in subjects with T1D to normal subjects.

Methods

This study is a descriptive-analytical and cross-sectional comparative study which conducted on 25 patients with T1D (12 males, 13 females) age ranging from 20 to 30 years (mean=25.1, SD=4.2) and 25 normal subjects (13 males, 12 females) aged 20 to 30 years (mean=23.23, SD =3.23). Patients were selected using available sampling method and they have referred from Endocrinology and Metabolism Research Center of Tehran University of Medical Sciences (TUMS) to Audiology Clinic of TUMS for hearing evaluation. The control group was matched according to age and sex. The inclusion criteria for the T1D group was being affected by T1D, age range 20-30 years, (hearing thresholds ≤15 dBHL in the frequency range of 250-8000 Hz, normal tympanogram with static compliance =0.1-3.6 cc and middle ear pressure of ±50 dapa and present acoustic reflexes [11], right handedness, no history of audiological and otological disorders, head trauma, neurological diseases such as epilepsy and multiple sclerosis, nerve disorders such as attention deficit disorder, and tinnitus, lack of sedative medication from 48 hours before the examination, not being a professional musician and filling out the consent form. After obtaining the consent, the required information was recorded in the history form, then, the Persian version of Edinburgh handedness questionnaire was used to ensure the right handedness of the subjects [12]. Also, the Persian version of the ASRS-v1.1 (Adult ADHD Self-Report Scale-V1.1) was used to rull out attention deficit disorder [13]. Then, the eligible subjects underwent otoscopy examination, pure tone audiometry (using AC40, Interacoustics, Denmark and immittance acoustic, Zodiac 901, Madsen, Denmark). After obtaining the inclusion conditions by individuals, the GIN test, the stimuli presentation, and the method of responding were explained to individuals, and in order to ensure complete justification, 10 stimuli were presented as a practice items. Finally, the gap in noise test was performed for each individual. The GIN test was performed in an acoustic chamber and the stimuli were recorded on a compact disk and played via a diagnostic audiometer (AC40, Interacoustics, Denmark). The stimuli included a series of broadband noise with a duration of 6 seconds. Which were presented at 50 dBSL (re: speech reception threshold) to each ear independently. Within this temporal range, there were several (zero to

three) random intervals of silence (gaps). The noise used in the test was white noise. The interstimulus intervals between noise segments were 5 seconds and the duration of intervals were 2, 3, 4, 5, 6, 8, 10 12, 15 and 20 ms. The duration and location of the intervals changed randomly, as well as the number of intervals in each noise segment, which prevented the patient from guessing. The shortest time between two intervals was 500 ms. the participants were asked to answer to the test by pressing the button as soon as they heard a gap. In that case, the answer would be considered correct. If they replied while there was no gap, the response was considered as false positive. The response was categorized as an error when there was a gap, but the button was not pressed. Each participant could have had two false positive responses in each ear, and the third false response was considered as an error and was not calculated in determining the percent correct answer [10].

The approximate threshold (ATh) and the percent correct answers were used for analysis. ATh was the shortest duration that the participant responded to at least 4 out of the 6 presentations. The two standard deviation (2SD) criterion (re: means of normal group) was used to determine subjects with abnormal responses [14]; this means that if the scores obtained by the participants two standard deviation different from the mean of the control group (for ATh higher cut-off and for the percent correct answers the lower cut-off), the individual was considered to have disorder in that criteria. Also, in this study, two factors that could possibly affect the responses were investigated. One was HbA1c levels that is a precise and sensitive biological index to determine how a person's disease is controlled over the past 2 to 3 months. The other factor was the duration of the disease.

Analyzing the data to examine the hypotheses was first conducted using the Kolmogorov-Smirnov test in terms of normal distribution, Mann-Whitney test was used to compare the mean of ATh between two groups of normal people and people with diabetes. Independent t-test was used to compare the percent correct answers between groups. The Wilcoxon test was also used to compare the mean of ATh between the right and left ears, and the pair t-test was used to compare the mean of the percent correct responses between the right and left ears. To compare the mean of ATh between women and men, was used Mann-Whitney test. Independent t-test were used to compare the mean percent correct responses between men and women. Also, in order to investigate the correlation between the ATh with HbA1c and the duration of the disease, we used Spearman's correlation coefficient, and Pearson correlation coefficient was used to examine the correlation between the percent correct response with HbA1c and the duration of the disease. Data analysis was performed using SPSS 22 at the significance level of 0.05.

Results

To study the effect of diabetes on auditory temporal processing, two components of GIN, ATh and the percent correct responses were compared between patients with T1D and normal group. There was a significant difference between the threshold and the correct answers of the GIN test of both ears between the two groups ($p<0.05$; Table 1).

There were significant difference between men with T1D and normal men ($p<0.05$) and also between women with T1D and normal women ($p<0.05$). The result have been shown in Table 2.

There was no significant difference ATh and the percent correct responses between women and men within each group (Table 2).

The results of descriptive statistics related to HbA1c levels and duration of disease as a central index and dispersion are presented in Table 3. Spearman Correlation test showed significant correlation between HbA1c and ATh. Pearson correlation coefficient test showed a relatively strong correlation between HbA1c and percent correct answers. Therefore with increasing HbA1c, ATh and the percent correct answers weakened (Table 4), there were no significant correlation between the duration

Table 1. Mean, median and standard deviation of the percent correct answers and the approximate threshold of gap in noise test in normal and type 1 diabetes groups

		Normal (n=25)		T1D (n=25)		
	Ear	Mean (SD)	Median	Mean (SD)	Median	p
Approximate threshold	**Right**	4.92 (0.57)	5	6.72 (0.97)	6	<.001
	Left	5.16 (0.55)	5	6.68 (1.02)	6	<.001
Percent correct answer	**Right**	68.53 (4.44)	68.33	59.86 (4.24)	60	<.001
	Left	67.86 (4.60)	68.33	58.93 (4.58)	60	<.001

T1D; type 1 diabetes

of the disease and ATh and the percent correct answers in all patients, both male and female, and in each ear (p>0.05).

According to the two standard deviation criteria, the cut-off values were 6.06 ms and 59.66% for ATh and the percent correct answers. In the control group, no one was diagnosed as abnormal with ATh and one participant was abnormal with the percent correct responses. In the T1D group, with ATh, 14 (56%) patients had disorder from among which 6 subjects (24%) had bilateral disorder, 4 subjects (16%) had the disorder in the left ear and 4 subjects (16%) had the disorder in the right ear. With the, the percent correct answers , 12 subjects (48%) had a disorder, among them, 6 subjects (24%) had the disorder in both ears and 4 subjects (16%) had the disorder in the left ear and 2 subjects (8%) had the disorder in the right ear.

Discussion

In this study, the mean of the approximate threshold and the percent correct responses of GIN in both ears were compared between normal individuals and patients with T1D. Since ATh has a higher sensitivity and specificity than the percent correct responses, only ATh has been calculated in some studies [15]. This means that with the percent correct responses, it is more likely that responses will fall within the normal range [14].

The findings of this study showed that there is a significant difference between the two ears between the mean ATh and the percent correct responses of normal group and patients with diabetes. So that the mean of ATh in normal group in both ears is lower than the mean threshold of the patients, and the mean percent correct responses in the normal subjects in both ears is greater than the mean of this component in people with T1D. This finding was also observed by eliminating the gender effect by comparing ATh and the percent correct responses of the GIN test separately in men and women. In spite of the different views regarding temporal resolution, it seems that at first the auditory cortex and then the brain stem have the greatest role in temporal resolution processing [16]. Also, studies that have investigated the temporal resolution processing in patients with lesion in the temporal lobe have shown the role of the temporal lobe in the processing of temporal resolution [17]. Studies on brain-induced waves have shown a significant reduction in brain activity in the temporoparietal section in people with T1D [6]. Also, imaging studies have shown that, during T1D, the density of gray matter in the parts of the brain, especially in the temporal region, is significantly reduced [18]. Regarding the role of auditory cortex and brain stem in temporal resolution processing and studies that have previously shown the destructive effect of T1D on these areas, it seems that the poor results of T1D patients in the GIN

Table 2. Mean of the approximate threshold and the percent correct answers of gap in noise test in each ears of men and women in normal and type 2 diabetic groups

			Normal			T1D			
	Sex	**Ear**	**N**	**Mean (SD)**	**Median**	**N**	**Mean (SD)**	**Median**	**p**
Approximate threshold	**Men**	**Right**	13	5.07 (0.493)	5	12	6.33 (0.77)	6	<.001
		Left	13	5.30 (0.48)	5	12	6.58 (1.08)	6	0.001
	Women	**Right**	12	4.75 (0.621)	5	13	7.07 (1.03)	8	<.001
		Left	12	5 (0.603)	5	13	6.76 (1.01)	6	<.001
Percent correct answer	**Men**	**Right**	13	67.43 (4.06)	68.33	12	61.52 (3.44)	62.49	0.001
		Left	13	67.17 (4.58)	68.33	12	60.55 (3.78)	60	0.001
	Women	**Right**	12	69.72 (4.70)	69.16	13	58.33 (4.46)	58.33	<.001
		Left	12	68.60 (4.70)	68.33	13	57.43 (4.88)	56.66	<.001

T1D; type 1 diabetes

test in this study are relevant to damaging these areas.

Although a similar study was not found with what was investigated in this study, a study was conducted on auditory temporal processing, and in particular the ability to time separation in type 2 diabetic patients, that apart from the type of test, its results are consistent with the results of the present study. Mishra et al., conducted the gap detection threshold test on 50 patients with type 2 diabetes at the age range of 30 to 40 years with hearing impairment at high frequencies in order to determine the ability of temporal resolution in individuals with diabetes type 2. The results indicated a significant weakness in the test results of diabetic patients in comparison to normal people [19]. The results obtained in this study are consistent with the results of studies conducted so far in the field of GIN test in normal people. Shinn et al. investigated the GIN test results in 72 normal children aged 7 to 18 years. They placed the children in 6 different age groups. The mean of ATh in different age groups was in the range of 4.1-5.36 ms, they also found that the results of this test do not vary in different age groups and are similar to those obtained in normal adults [14]. Zaidan et al. compared the performance of 25 individuals aged 18 to 29 years in two tests of GIN and random gap detection. None of participants had a history of academic, neurological or linguistic problems. The mean approximate thresholds in the left and right ears were 5.38 and 4.88 ms, respectively [20]. In a study conducted by Musiek et al., 50 normal subjects were evaluated, the average approximate threshold in the right and left ears were 4.9 and 4.8 ms, respectively, and the percent correct responses were 70.3% and 70.2% respectively [21].

Another purpose of this study was to investigate the effect of gender in normal and diabetic subjects on ATh and the percent correct responses of the GIN test. The results show that, in general, the difference between the average threshold and the percent correct responses of the GIN test in both ears are not statistically significant in comparing the normal men to the normal women. In the diabetes group, the means of the approximate threshold and the percent correct responses of the GIN test in both men and women in the left and right ear are not significantly different. These findings are consistent with the results of Sharifinik et al. [22], and Valadbeigy et al. [23].

It was found that in the normal group, there was no statistically significant difference between

Table 3. Statistical values of HbA1c and duration of disease in patients with type 2 diabetic (n=25)

	Mean (SD)	Median	Min	Max
HbA1c(%)	7.41 (0.52)	7.5	6	8
Duration (years)	9.36 (4.11)	9	1	19

the two ears in both male and female groups. In the T1D group, there was no statistically significant difference between the results of the two ears and in both women and men in any of the GIN test criteria. These findings are consistent with the results of previous studies, including Perez and Pereira [24], Shinn et al. [15], Balen et al. [25], Museik et al. [21]. Also Efron et al. [17] investigated the gap detection tasks in 56 normal individuals, and observed similar performance between the two ears. The results of this study are similar to most of the previous findings. In fact, several studies that have examined the GIN test in different populations did not report ear dominance. Although there may be a difference between the right and left ear in the ability of differentiating temporal resolution, but not all the methods for evaluating the temporal resolution do istinguish the difference. Studies that used the GIN test have, confirmed this finding. GIN is administered monaurally, and activates both the ipsi- and contralateral auditory pathways, which results in similar function in the two ears [26,27].

Table 4. The correlation between the approximate threshold and the percent correct answers with HbA1c in patients with type 1 diabetes (n=25)

	Ear	Sex	N	r (p)
Approximate threshold	**Right**	**Men**	12	0.592 (0.042*)
		Women	13	0.768 (0.002*)
	Left	**Men**	12	0.814 (0.001*)
		Women	13	0.596 (0.032*)
Percent correct answer	**Right**	**Men**	12	-0.776 (0.003**)
		Women	13	-0.742 (0.004**)
	Left	**Men**	12	-0.635 (0.027**)
		Women	13	-0.806 (0.001**)

* Spearman
** Pearson

In the present study, the correlation between the components of GIN tests and HbA1c has been evaluated. The goal was to determine if higher HbA1c can lead to abnormal results of GIN. The findings of this evaluation indicate that the measure of HbA1c has a good positive correlation with the threshold of GIN in both ears and in both sexes, and this correlation is statistically significant. We found a significant negative correlation between the percent correct responses of the GIN test with the HbA1c. The study of the role of glycemic control is very complicated since, on the one hand, proper and good blood glucose control can prevent involvement of the central nervous system, and, on the other hand, the very severe metabolic control to keep blood glucose levels lower and to prevent the destructive effects of hyperglycemia, generally accompanies with hypoglycemia [28] that the attacks themselves potentially have very damaging effects on the brain. These two-dimensional effects of glycemic control occur especially at early stages of severe insulin therapy [29].

The duration of the disease is another factor, which is considered in this study. The purpose of the study was to examine the correlation between the duration of the disease and the components of the GIN test to determine if the patients who have had dealt more time with this disease are more likely to be affected by temporal processing disorders. Accordingly, this correlation has been evaluated in patients in terms of sex and in both ears. The findings showed that there is no significant correlation between the duration of the disease and the components of the GIN test. Although a similar article was not found that investigates the duration of diabetes with auditory temporal processing, a number of papers on peripheral hearing assessment in patients with T1D indicate that the duration of the disease has no effect on the increasing of the severity of hearing loss

[30,31].

One of the limitations of this study was the lack of otoacoustic emissions (OAE) recording in studying the cochlear lesions associated with normal hearing, as Oxenham and Bacon argued, even small cochlear lesions may interfere with the cochlear amplification mechanism and affect the auditory temporal resolution skill [32].

Conclusion

The results of the present study indicate that T1D patients had abnormal results in GIN temporal processing tests. These results may in some way indicate a possible defect in the ability of temporal processing in these patients. In this study, it was indicated that in patients with T1D, the mean of the approximate threshold of GIN test was significantly increased and the percent correct responses to GIN tests was significantly reduced in comparison to the normal group.

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Conflict of interest

The authors declared no conflicts of interest.

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