Research Article

Evaluation of Synaptopathy by Use of Latency Shift of Wave V Auditory Brainstem Response in the Presence of Ipsilateral Noise

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Citation: Sabzinasab Z, Rouzbahani M, Toufan R, Maarefvand M. Evaluation of Synaptopathy by Use of Latency Shift of Wave V Auditory Brainstem Response in the Presence of Ipsilateral Noise. Aud Vestib Res. 2023;32(1):47-53.

https://doi.org/10.18502/avr.v32i1.11321

Highlights

- Latency of wave V increased with increasing noise levels in both groups
- Only at 40 dB, there is a significant relationship between the two groups
- People with no noise exposure had a faster latency increase than those exposed ones

Article info:
Received: 21 Jan 2022
Revised: 14 Jun 2022
Accepted: 02 Jul 2022

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ABSTRACT

Background and Aim: Recreational and occupational noise can cause permanent damage to the inner ear. Cochlear synaptopathy can be "hidden" because this synaptic reduction can occur without permanent hearing threshold changes. Our study aimed to assess synaptopathy in people with and without a history of occupational noise exposure by use of latency shift of wave V with masking.

Methods: In this study, 38 males were involved. All participants had normal hearing thresholds. Of 38 males, 20-male identified with exposure to occupational noise and 18 identified without occupational noise exposure. Auditory brainstem response and masked were performed.

Results: The main effect of the between-group factor was not significant in the right and left ears. But the main effect of the within-group factor in the right and left ears were significant ($p<0.001$ and $p<0.001$). Auditory brainstem response latencies at different levels in each group were significant. These results showed that there were no significant differences between latency changes in both groups.

Conclusion: In order to diagnose cochlear synaptopathy in humans it is important to use audiological test batteries in the future. There is currently no effective way to diagnose noise-induced cochlear synaptopathy in human subjects.

Keywords: Noise induce cochlear synaptopathy; auditory brainstem response; cochlear synaptopathy; hidden hearing loss

Introduction

Recreational and occupational noise can cause permanent damage to the inner ear [1]. From the crowded classroom to the crowded restaurant, our world is a noisy place [2]. Until now, it was thought that only exposure to loud noises could damage the hearing system [3]. Evidence from human and animal studies suggests that exposure to moderate sounds can cause a temporary increase in the threshold and interfere with the encoding of suprathreshold sounds [4].

Recent preclinical studies suggest that synapses between inner hair cells and Low Spontaneous Rate (LSR) spiral ganglion neurons (i.e. high threshold fibers) are the most vulnerable subcellular structures to aging and noise exposure [5, 6]. This Cochlear Synaptopathy (CS) can be "hidden" because this synaptic reduction can occur without permanent hearing threshold changes [7]. Although LSR fibers are not involved in stimulus detection in silence, they do participate in the detection of transient stimuli in the presence of continuous background noise [8]. Scientists have believed for decades that the first indicator for the death of outer hair cells were tinnitus and noise-induced hearing loss [9]. It has been shown in an animal study that permanent damage to auditory nerve fibers can be caused by exposure to noise, even if the threshold change is not permanent and Outer Hair Cells (OHC) performance return [9]. Changes in Distortion Product Otoacoustic Emission (DPOAE) and Auditory Brainstem Response (ABR) thresholds are not permanent, even a reduction of up to 50% of spiral ganglion cells [6, 9].

Of the adults who visit an audiologist for hearing impairment, 5 to 15 percent have normal hearing [10].

However, the standard hearing assessment would not be sufficiently sensitive to CS [11]. Therefore, it is essential to do conventional audiological tests with new approaches for the CS and use new audiological test batteries in the future if their clinical evidence is optima [12].

One of the electrophysiological measures most commonly used as a marker for CS is the amplitude of wave I in ABR [12]. However, there are limitations to this test. First, in this test, the amplitudes in humans are less than those recorded in animals[13]. Second, there is significant variability among subjects regarding the amplitude of wave I [3]. Third, while the amplitude of wave I have excellent test-retest reliability in humans, its inter-subject standard deviation is quite large [3].

A recent study has utilized the latency shift of wave V as a marker for CS. Mehraei et al. evaluated the use of a masking noise while measuring wave V latency. In this study, 23 normal-hearing individuals from Boston University and the Massachusetts Institute were selected. In masked ABR 80μs clicks at 80 dB peSPL with broadband noise varying from 42 to 82 dB SPL in 10 dB steps were used. Their study evaluated the use of a masking noise while measuring wave V and found an increased latency of wave V with masking [4].

In a study conducted by Atias and Pratt, in people with a history of occupational noise exposure, it was shown that the latency of waves III and V in ABR, increases only at a rate of 55 per second [14]. Another study by Almadori et al., on people with a history of occupational noise exposure, showed that the latency of waves I, III and V was in the normal range [15].

All the above-mentioned research might indicate the possible effect of noise exposure on the latency of waves in ABR in cases where they might be at risk of CS. In Mehraei et al. study [4], results of ABR have been obtained in two situations; with and without masking. In two other studies [14, 15], results have been obtained without masking.

The purpose of this study was to evaluate synaptopathy in people with and without a history of occupational noise exposure by use of latency shift of wave V with masking.

Methods

Participants

All tests were performed in the Mirdamad office of Ettelaat newspaper and School of Rehabilitation Sciences, Iran University of Medical Sciences. All volunteers were accepted to participate by providing written consent.

All participants were male because all workers in the Ettelaat newspaper environment were male. In each test, the responses were recorded separately for each ear. Inclusion criteria in this study were normal hearing thresholds and passing the DPOAE test. In this study38 male participants with a mean(SD) of age 33.66(4.78) were involved. To compare the differences between both groups at each level, post-hoc Tukey's was used. To calculate the sample size, the means and SD were used. The power was set at 0.8 and the level of significance was 0.05.

Otoscopy (Heine, Germany) was done to ensure that ear canals were clear and unobstructed and both tympanic membranes were intact in all participants. Audiometry test revealed normal hearing thresholds (≤20 dB HL) at octave frequencies from 250 to 8000 Hz as well as 3000 and 6000 Hz. In this study, we used a screening and AC40 audiometer (interacoustic, USA) for the assessment of hearing thresholds. DPOAEs were recorded from both ears for all participants using Maico (Germany) apparatus, a screening DPOAE system. Depending on the size of the ear canal, a suitable probe was used, and all participants had normal OHC function according to DPOAE test results.

Of 38 men who participated in the study, 20 identified with exposure to occupational noise (experimental) and 18 without occupational noise exposure (control) based on data in the office of Ettelaat newspaper.

The auditory brainstem response test was performed using Vivosonic (USA) system. Both ears were tested. The inverting electrode was placed on the mastoid of the ear that received the stimulus and ground electrode was placed on the mastoid of the opposite ear and the noninverting electrode was placed on the top of the forehead. All electrode impedances were less than 5 kΩ. The impedance difference between electrodes was maintained at 2 kΩ. Stimuli for ABR recording were clicks of 80 dB nHL presented at a rate of 11.1/s with rarefaction polarity. Masked ABRs were recorded after delivering broadband noise with the intensity of 40 to 80 dB nHL in the steps of 10 dB (click and ipsilateral noise were presented through a two-pronged probe). A minimum of 2000 accepted trials per run were obtained, averaged, and stored. In order to control ocular and muscular artifacts, after the artifact rejection was kept at a low level, individuals were asked to perform the following:

being relaxed, closing the eyes, sleeping if possible, immobility.

Results

This study aimed to assess hidden hearing loss in people with exposure to occupational noise. In this study, 38 male participants were involved. The data from ABR were analyzed in SPSS version 17. Q-Q plot showed that data were distributed normally.

The mean and standard deviation for the latency of wave V shifted with increasing background noise levels (40, 50, 60, 70, and 80) at 80 dB nHL click are presented in Table 1. The result showed that the latency of wave V increased with increasing noise levels in both groups. On average, the mean latency of wave Vin the experimental group was higher than in the control group and the mean latency of wave Vin the right ear was higher than in that of the left ear, although there were few differences, these differences were not significant in both ears.

Mixed ANOVA was performed with factors of the ear (left and right) as a within-group factor, and group (experimental, control) as a between-group factor. The main effect of between-group factors was not significant in the right and the left ear ($p=0.062$ and $p=0.354$ respectively). The main effect of within-group factors in the right and the left ear was significant ($p<0.001$and $p<0.001$). These results are shown in Table 1. Figure1 showed the latency shift of wave V with masking in both groups. There were no significant differences between latency changes in both groups.

In both groups, the latency of wave V increases with increasing masking level but the difference of latency in increasing of 10 dB is not significant.

Examining the slope of the latency intensity function at different noise intensities in Figure 1, it can be seen that people who were not exposed to noise had a faster latency increase than the group with a history of noise exposure. However, this correlation is not significant; only at 40 dB was a significant ($p<0.03$) relationship between both groups. In Figure 2 experimental group is significantly higher than the control group, but at other intensities, this relationship is not significant and at 80 dB they are quite similar.

Discussion

In this study, normal hearing young men with and without a history of occupational noise exposure were evaluated to determine if there was a link between noise exposure and latency shift of wave V in the presence of ipsilateral noise.

In previous studies to investigate the presence of synaptopathy or hidden hearing loss, different electrophysiological criteria in animals and humans have been used such as latency shift of wave V in ABR, the amplitude of wave I in ABR [4, 16-19], Envelope Following Response (EFR) [17], Electrocochleograghy [20] Frequency Following Responses (FFR) [21].

In a recent study, Mehraei et al's study investigate synaptopathy using ABR by masking. Who in part used

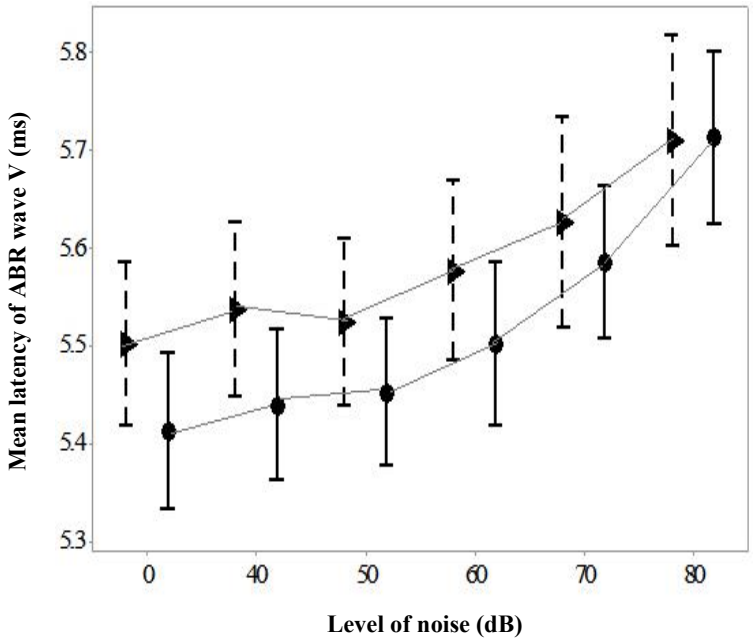

Figure 1. Means and confidence interval for the latency of wave V as a function of noise level in both experimental (arrow and broken line) and control (circle and continuous line) group. ABR; auditory brainstem response

ABR to investigate synaptopathy and hidden hearing loss and found that masked ABRs showed evidence of increasing latency of wave V. Also in another part of their study on animals [4] they examined whether noise-induced affects how the latency shift of wave IV with increasing background noise level or whether the shift in latency of wave IV (similar wave V latency in humans) was measured in mice when a 60 or 80 dB SPL broadband mask was added to the tone pipe stimulator. They found that mice with histologically confirmed noise-induced synaptopathy showed a smaller latency shift than control mice by adding a mask, especially for a 60 dB SPL mask. They stated that this smaller latency shift indicates a loss of LSR fibers because LSR fibers are more resistant to background noise and have a delayed onset response compared to High Spontaneous Rate (HSR) fibers.

In this study, latency shift of wave V with an increase in noise was chosen and high-intensity click was used to stimulate LSR fibers specifically. These fibers have higher thresholds than HSR fibers. Therefore, the change in latency of wave V can reflect the activity of LSR fibers because they have a delayed initiation re-

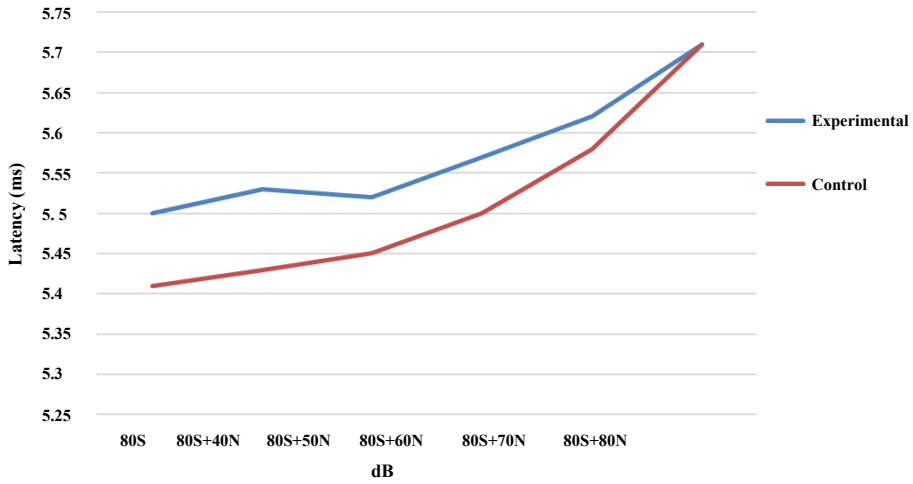

Figure 2. The effect of masking noise on auditory brainstem response waves in control and experimental groups. In this figure, 80 signal referred to a level that click ABRs were presented and S reffered to signal.

Table 1. Descriptive statistics for the latency of wave V auditory brainstem response with noise in the both groups

Ear	Level of noise (dB)	Experimental group			Control group	Min (ms)	Max (ms)
		Mean(SD) (ms)	Min (ms)	Max (ms)	Mean (SD) (ms)		
Right	0	5.50(0.26)	4.95	6.10	5.38(0.24)	5.01	5.84
	40	5.55(0.28)	5.01	6.20	5.42(0.21)	5.06	5.79
	50	5.55(0.29)	5.06	6.31	5.45(0.19)	5.11	5.74
	60	5.60(0.26)	5.27	6.20	5.50(0.26)	5.11	6.00
	70	5.64(0.31)	5.21	6.46	5.56(0.24)	5.21	5.94
	80	5.71(0.32)	5.21	6.41	5.71(0.29)	5.27	6.41
Left	0	5.49(0.26)	4.95	6.05	5.43(0.23)	5.06	5.84
	40	5.52(0.27)	5.06	6.26	5.45(0.24)	5.01	6.00
	50	5.49(0.24)	5.11	6.05	5.48(0.23)	5.01	6.00
	60	5.54(0.31)	5.01	6.31	5.49(0.23)	5.01	5.94
	70	5.60(0.36)	5.06	6.67	5.60(0.22)	5.21	6.10
	80	5.70(0.35)	5.11	6.67	5.71(0.22)	5.27	6.20

sponse compared to HSR fibers and are more resistant to background noise. With using masking, HSR fibers become asynchronous and are removed from ABR, because they are sensitive to noise, while LSR fibers are more resistant to noise and participate in ABR response, but these fibers have increased latency, so the response is associated with increased latency. Selective loss of fibers with LSR should result in smaller ABR delay changes as the noise level increases.

Since the latency changes function in both groups is nonlinear, it is not possible to compare the slope of the two functions; therefore, we made a comparison at two points: 1) low noise intensity level (40 dB) and 2) high noise intensity levels. There was a significant difference in low noise levels (40 dB), but we did not see this significant difference in high noise levels.

We found no significant difference in the rate of change and the slope of the function in the control and experimental group. In the control group, latency increases rapidly, while latency changes in the experimental group are not rapid, and this significant difference is not maintained at high-intensity levels.

The paradoxical response of the central nervous system can take the form of an increase in response to environmental deprivation; it is not possible to interpret the full form of data in that format, and we must still consider complex central interactions in other studies. Therefore, it is not clear whether and how central changes affect the change in latency of wave V with noise levels and how these effects are related to cochlear synaptopathy.

In this study, all participants were men because synaptopathy is affected by gender.

Differences between our study and Mehraei et al. study [4] may be due to the prevalence of noise-induced cochlear synaptopathy may not be high in young people in our study, NICS may only be common for low-intensity stimuli, and tests using higher-intensity stimuli do not show major anomalies [21].

The effect of noise exposure was assessed on the latency of wave V in this study since it may increase the possibility of degeneration in synaptic connections between auditory nerve fibers and hair cells which can be due to moderate noise exposure [22]. Following the destruction of the synapse, the auditory nerve fiber is turned off, while the cellular body may be alive. This diffuse nerve damage may reduce the processing aspects of the supra threshold hearing, but this has no effects on conventional hearing thresholds [17]. This process is called synaptopathy, which leads to hidden hearing loss, while

noise-induced hearing loss is due to changes in hearing sensitivity or threshold changes [23].

We need to consider the limitations of audiometric testing as an audiological assessment system. NICS identification is dependent on cochlear histology; thus, there are very few studies in which cochlear synaptopathy has been confirmed in humans.

Conclusion

The use of latency shifts of wave V auditory brainstem response in the presence of ipsilateral noise did not confirm the occurrence of synaptopathy in the human population following noise exposure. Higher noise in the experimental group was different with a lower slope but was not significant. These results indicate the need to use a test battery to evaluate synaptopathy and to conduct further studies to document the effects of noise on the auditory system of humans.

Ethical Considerations

Compliance with ethical guidelines

This study was approved by the Ethics Committee of Iran University of Medical Sciences (IR.IUMS.REC.1398.1372).

Funding

This research did not receive any grant from funding agencies in the public, commercial, or non-profit sectors.

Authors' contributions

ZS: Acquisition of data, interpretation of the results, and drafting the manuscript; MR: Study design,interpretation of the results, revising the manuscript; RT: Study design, drafting the manuscript; MM: Statistical analysis, interpretation of the results, drafting the manuscript.

Conflict of interest

The authors declare that they have no conflicts of interest.

Acknowledgements

Thanks to Mirdamad office of Ettelaat newspaper for referring the case for this study.

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