Research Article



Auditory Brainstem Response Patterns in Misophonia: A Comparative Study

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Highlights

- Auditory brainstem response findings were compared between controls and misophonia
- Individuals with misophonia showed shorter absolute latencies at 11.1/s stimulus rate
- It shows altered sub-cortical auditory processing in individuals with misophonia

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ABSTRACT

Background and Aim: Misophonia is a condition characterized by a reduced tolerance to certain sounds or the stimuli linked to those sounds. Our study aimed to investigate the auditory brainstem functioning using electrophysiological measures in normal-hearing individuals with and without misophonia.

Methods: Thirty participants aged between 18 and 30 years were recruited. They were divided into two primary groups: fifteen individuals diagnosed with misophonia and fifteen controls. The selection of participants with misophonia was based on the diagnostic criteria by Schröder et al. and the MisoQuest questionnaire; Auditory Brainstem Response (ABR) was recorded from all the individuals at lower (11.1/s) and higher stimulus rates (90.1/s).

Results: On analysing the data, individuals with misophonia showed significantly shorter absolute latencies of ABR waves III and V at 11.1/s. Also, there was no significant difference in the absolute amplitude of ABR waves at 11.1/s and 90.1/s between the individuals with and without misophonia.

Conclusion: This study indicates that the shorter absolute latencies of ABR waves III and V in individuals in misophonia could be attributed to hyperactivity at the sub-cortical pathway regions compared to the control group.

Keywords: Misophonia; auditory brainstem response; hyperactivity

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Introduction

he term "misophonia" originates from the Greek words "misos", meaning hatred, and "phónè", meaning sound. Over time, the term misophonia has become the predominant term to describe this condition, as evidenced by recent studies [1, 2]. This term encapsulates the core characteristic of the phenomenon, referring to the intense adverse emotional and physiological reactions associated with Decreased Sound Tolerance (DST) [3, 4]. Misophonia is a relatively recent concept in audiology and psychology, having gained recognition only in the past few decades. The hallmark of misophonia is the presence of extreme adverse responses to specific auditory stimuli, referred to as "triggers". These triggers can provoke many emotional and physiological reactions [5]. These triggers may involve specific auditory, visual, or audiovisual stimuli [1, 5]. Human-produced sounds, such as breathing, chewing, lip-smacking, and swallowing, can serve as unpleasant auditory triggers. Repetitive movements such as leg shaking or the appearance of lips moving while chewing can be visual triggers [1, 5]. Additionally, sounds unrelated to the human body, like clicking, rustling, and typing, can also function as auditory triggers [1, 5]. Misophonia is a condition that draws from audiology, neurology, and psychiatry, yet lacks clearly defined diagnostic criteria and standardized assessment protocols across these fields [4, 5]. Although the condition has garnered increasing attention in recent years, the scientific community has yet to reach a consensus on the most effective methods for diagnosis and treatment [6]. Studies examining the prevalence of misophonia have been conducted in diverse populations across various countries, including students and the general public. In Western nations, reported prevalence rates range from 4.6% to 54% [7, 8], while in India, the prevalence is estimated to range from 15% to 34% [9-13].

While the focus of audiological assessment in individuals with misophonia has traditionally been subjective tests, a few studies have explored objective testing using auditory evoked potentials [14-20]. A study by Kim et al. reported an enhanced wave I Auditory Brainstem Response (ABR) amplitude in individuals with misophonia and a prolonged wave V latency compared to individuals with hyperacusis and

control subjects [20]. In contrast, Aryal and Prabhu found no statistically significant differences between individuals with misophonia and other groups in ABR amplitudes, absolute latencies, or interpeak latencies. The result of their study suggests that individuals with misophonia may exhibit normal neuronal synchrony up to the brainstem regions [21]. However, Aryal and Prabhu included only individuals with mild to moderate misophonia, leaving the potential for variations in brainstem processing unexamined in individuals with more severe forms of the disorder [21].

Similarly, Kim et al. did not report the severity of misophonia in their sample [20]. Consequently, it is possible that variations in brainstem processing could be associated with the severity of misophonia, with individuals exhibiting more severe symptoms potentially demonstrating abnormal processing at the brainstem level. Therefore, it can be hypothesized that neural processing up to the brainstem level could be altered among individuals with misophonia. This altered neural activity may contribute to the heightened sensitivity to sound stimuli observed in more severe cases of misophonia, potentially resulting from impaired processing of auditory signals at the brainstem [22, 23]. Considering the disparities in findings from previous studies, further research exploring the auditory brainstem functioning in individuals with misophonia having higher severity is warranted.

Electrophysiological measures, such as ABR testing, could provide more definitive insights into the neural mechanisms underlying this condition. Hence, the study aimed to assess auditory brainstem functioning using electrophysiological measures in individuals with and without misophonia. Specifically, the objective is to compare the ABR parameters, including latencies and amplitudes, elicited by clicks at stimulus rates of 11.1/s and 90.1/s between individuals with misophonia and a control group without the condition.

Methods

Study participants

A standard group comparison with purposive sampling was applied in this study. A total of thirty participants aged between 18 and 30 years were

recruited. The participants were divided into two primary groups: fifteen individuals diagnosed with misophonia (12 females, 3 males) (mean age: 23.25 years, SD: 2.89 years) and fifteen controls (9 females, 6 males) (mean age: 23 years, SD: 2.80 years). In the misophonia group, ten individuals had a moderate degree of misophonia, and five had severe misophonia. The selection of participants with misophonia was based on the diagnostic criteria by Schröder et al. [24] and the MisoQuest questionnaire, as described by Siepsiak et al. [25]. The severity of misophonia was assessed using the Revised Amsterdam Misophonia Scale (RAMISO-S) [26]. RAMISO-S scores were classified as follows: 0-10 indicating no misophonia (subclinical), 11-20 indicating mild misophonia, 21–30 indicating moderate misophonia, and 31-40 indicating severe misophonia. Individuals scoring ≤10 were excluded; only those scoring 21 or higher were included in the study.

Exclusion criteria were as follows: participants with significant history of otological disorders, prolonged or frequent exposure to loud noise, alcohol consumption, smoking, ototoxic drug use, a family history of hearing loss, or any other medical conditions that might influence the study outcomes. Additionally, participants with tinnitus were excluded through the administration of the Tinnitus Handicap Inventory (THI), while those with hyperacusis were excluded using the Modified Khalfa Hyperacusis Questionnaire (MKHQ) [27, 28].

Procedures

Prior to audiological evaluations, a comprehensive case history was collected from each participant to screen for any otological issues, hearing impairments, or histories of noise exposure. The participants were first evaluated through otoscopy to check for outer ear and ear canal anomalies. This was followed by standard Pure Tone Audiometry (PTA), Immittance Evaluation (IE), and Distortion Product Otoacoustic Emissions (DPOAEs) to ensure normal hearing sensitivity, middle ear function, and outer hair cells functioning, respectively. All the testing procedures were carried out in a randomized order for both ears.

Pure tone audiometry

Air conduction thresholds were measured using a calibrated two-channel clinical audiometer, the Inventis

Piano (Inventis Padova, Italy), with Telephonics Dynamic Headphones 39 earphones fitted with MX-41/AR supra-aural ear cushions. Bone conduction thresholds were obtained using the Radio Ear B-71 bone vibrator. The criterion for normal hearing sensitivity was defined as ≤15 dB HL at octave frequencies from 250 Hz to 8000 Hz for air conduction and 250 Hz to 4000 Hz for bone conduction, based on the modified Hughson-Westlake procedure [29].

Immittance evaluation

An immittance evaluation was performed using a Grason-Stadler Tympstar Pro immittance meter to assess middle ear function (Grason Stadler, Inc., MN, USA). Tympanometry was administered with a probe tone of 226 Hz at 85 dB SPL, and acoustic reflexes were measured at 500, 1000, 2000, and 4000 Hz frequencies. All participants exhibited 'A' type tympanograms with present acoustic reflexes at 500 and 1000 Hz, as reported in previous studies [30].

Distortion product otoacoustic emissions

DPOAEs were measured using the Otodynamics DP Echoport otoacoustic emission instrument (ILO292-USB-II, V6), with measurements at octave and mid-octave frequencies between 1 kHz and 6 kHz. A Signal-to-Noise Ratio (SNR) of +6 dB at three consecutive frequencies indicated the presence of otoacoustic emissions [31]. All participants met the inclusion criteria and underwent ABR testing.

Testing environment

All procedures were conducted in an acoustically treated room, adhering to the noise level standards specified by the American National Standards Institute (ANSI) Acoustical Society of America (ASA) ANSI/ASA S3.1-1999 [32].

Auditory brainstem response

ABR was recorded using the calibrated fourchannel SmartEP Intelligent Hearing Systems (IHS, Miami, FL). Electrodes were placed according to the 10–20 International System: one positive electrode at Fz (high forehead), two negative electrodes at the right (M2) and left (M1) mastoid regions, and a ground

electrode at FPz (lower forehead) [33]. Impedance levels were maintained below 5 k Ω for absolute impedance and 2 k Ω for inter-electrode impedance [34, 35]. In this study, stimuli were presented at a single intensity level of 80 dB nHL, as this higher intensity, coupled with a higher stimulation rate (90.1/s), helps detect retrocochlear lesions, including abnormalities in the auditory nerve and brainstem structures [34]. Before the ABR testing, the participants were provided the test stimuli (clicks) at 80 dB nHL and ensured that the intensity was tolerable and did not cause any discomfort for all the participants. Two repetitions of 1500 sweeps were recorded for each rate for reliable recordings [34, 35]. A binaural ABR was recorded for each participant. Stimulus and acquisition parameters are provided in Table 1.

Statistical analyses

The statistical analysis was conducted using IBM SPSS Statistics (version 26, IBM Corp., Armonk, NY). The data distribution was assessed using the Shapiro-Wilk test of normality, which revealed a non-normal distribution (p<0.05). Consequently, non-parametric tests were employed to further analyze the data.

Results

Auditory brainstem response findings

The absolute latency, inter-peak latencies, and amplitudes of ABR waves I, III, and V were measured at 11.1/sec, and the absolute latency and amplitude of wave V were measured at 90.1/s. These parameters were recorded and tabulated for subsequent statistical analysis. ABR waves I and III were absent at a stimulus rate of 90.1/s in most participants; therefore, these parameters were excluded from the analysis.

Comparison of absolute latency in individuals with and without misophonia

The results of the absolute latencies were subjected to a descriptive statistical analysis. Results showed that absolute latencies of waves III and V arrived earlier at 11.1/s in individuals with misophonia than in control groups. The absolute latencies of wave I at 11.1/s and wave V at 90.1/s were similar between the two groups.

The median, quartiles, minimum, and maximum of absolute latencies of all the ABR waves at 11.1/s are represented in Figure 1.

Table 1. Stimulus and acquisition parameters for auditory brainstem response for Clicks

Stimulus Parameters		
Type of stimulus	Clicks	
Duration of stimulus	100 μs	
Polarity	Rarefaction	
Repetition rate	11.1/sec and 90.1/sec	
Intensity	80 dB nHL	
Sweeps	1500	
Mode	Binaural	
Acquisition parameters		
Analysis time	12 ms	
Amplification	1,00,000x	
Filter	High pass (HP) 100 Hz–low pass 3 kHz	
Electrode montage	Vertical (Fz, Fpz, M1, M2)	
Electrode impedance	$<5 \text{ k}\Omega \text{ (absolute)} <2 \text{ k}\Omega \text{ (inter electrode)}$	
No. of channels	2	

The mean, Standard Deviation (SD), and results of the Mann-Whitney U test for absolute latencies (ms) of all the waves of ABR are provided in Table 2.

Furthermore, Mann-Whitney U tests were conducted to see the differences between the two groups. Mann-Whitney U test results showed a statistically significant difference (p<0.05) in ABR parameters, such as the absolute latencies of wave III and V at 11.1/s for individuals with misophonia compared to the control group. However, the results showed no statistically significant difference (p>0.05) in absolute latencies of wave I at 11.1/s and wave V at 90.1/s.

The grand averaged waveforms of recorded ABR for control and misophonia group at 11.1/s are shown in Figure 2.

Comparison of Absolute amplitude in individuals with and without misophonia

The results of the absolute amplitude were subjected to a descriptive statistical analysis. Results showed that the two groups' absolute amplitude of waves I, III, and V at 11.1/s and the absolute amplitude of wave V at 90.1/s were similar.

The median, quartiles, minimum, and maximum of absolute amplitude of all the waves of ABR at 11.1/s are represented in Figure 3.

The mean, standard deviation, and results of the Mann-Whitney U test for absolute amplitude (μV) of all the waves of ABR are provided in Table 3.

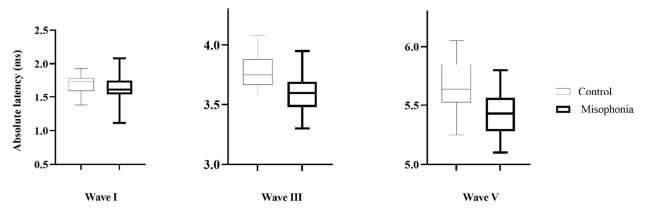


Figure 1. Median, quartiles, minimum, and maximum of absolute latencies (ms) of all the auditory brainstem response waves at 11.1/s

Table 2. The mean, standard deviation, and results of the Mann–Whitney U test for absolute latencies (ms) of all the waves of auditory brainstem response between the two groups (n=30)

Repetition rate	Parameter	Group	Mean(SD)	Inferential statistics
11.1/s	Wave I latency	Control	1.69(0.13)	U=340.0
	Wave I latency	Misophonia	1.64(0.19)	Z=1.62, p>0.05
	Wave III latency	Control	3.79(0.16)	U=241.0
	Wave III latency	Misophonia	3.66(0.28)	Z=3.09, p<0.05
	Wave V latency	Control	5.66(0.21)	U=201.5
	Wave V latency	Misophonia	5.44(0.21)	Z=3.67, p<0.05
90.1/s	Wave V latency	Control	6.22(0.15)	U=380.0
	Wave V latency	Misophonia	6.12(0.31)	Z=1.03, p>0.05

U; test statistics, Z score; standardized U statistic, p; significance value

Furthermore, Mann-Whitney U tests were conducted to see the differences between the two groups. Mann-Whitney U test results showed no statistically significant difference (p>0.05) in the absolute amplitude of waves I, III, and V at 11.1/s and wave V at 90.1/s between the two groups.

Comparison of Interpeak latency in individuals with and without misophonia

The results of the interpeak latencies were subjected to a descriptive statistical analysis. Results showed that interpeak latencies of wave I-V were earlier at 11.1/s in individuals with misophonia compared to control groups. The interpeak latencies of wave I-III and III-V at 11.1/s were similar between the two groups.

The median, quartiles, minimum, and maximum of interpeak latencies (ms) of all the ABR waves at 11.1/s are represented in Figure 4.

The mean, standard deviation, and results of the Mann-Whitney U test for interpeak latencies (ms) of all the waves of ABR are provided in Table 4.

Furthermore, Mann-Whitney U tests were conducted to see the differences between the two groups. Mann-Whitney U test results showed significantly earlier interpeak latency I-V (p<0.05) and no statistically significant difference (p>0.05) in the interpeak latencies of wave I-III and III-V at 11.1/s between the two groups.

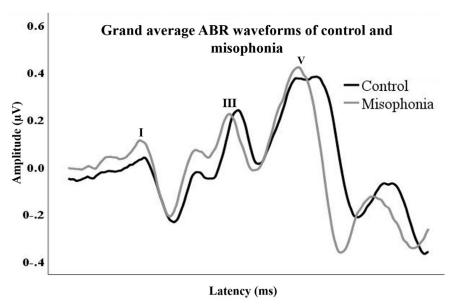


Figure 2. Grand averaged waveforms of recorded auditory brainstem response for control and misophonia group. ABR; auditory brainstem response

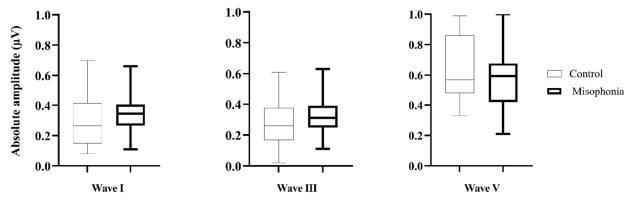


Figure 3. Median, quartiles, minimum, and maximum of absolute amplitude (μV) of all the auditory brainstem response waves at 11.1/s

Discussion

The current study explored the ABR in individuals with and without misophonia. The results indicate that individuals with misophonia exhibited earlier absolute latencies for waves III and V at a stimulus rate of 11.1/s. In general, latency denotes the timing of responses from neural sources [34, 35]. Wave III and IV originate at the cochlear nucleus and superior olivary complex. Wave V is majorly generated in the lateral lemniscus and inferior colliculus [34, 35]. Hence, the results of our study suggest a possible hyperactivity at these sub-cortical centers in individuals with misophonia. The absolute latencies of wave III and V at 80 dB nHL and 11.1/s stimulus rate could be a good indicator of the unique trend of ABR in those with misophonia. Also, these results support our hypothesis that misophonia is associated with altered sub-cortical auditory processing. However, the similar latencies for wave I at 11.1/s suggest that the peripheral auditory system, which includes the cochlea and the auditory nerve, may not be significantly different between the two groups.

Specifically, the earlier latencies of these waves indicate the heightened response to the auditory stimuli in individuals with misophonia. It is speculated that the neural hyperactivity at the sub-cortical auditory regions such as the cochlear nucleus, superior olivary complex, lateral lemniscus, and inferior colliculus contributes to the heightened response. These findings align with the previous study by Aryal and Prabhu which reported that the latency of p1 and n1 peaks of cortical auditory evoked potentials are significantly shortened in individuals with misophonia. They stated that there could be a possible existence of altered auditory processing within specific brain regions that generate these peaks among

Table 3. The mean, standard deviation, and results of the Mann-Whitney U test for absolute amplitude (μ V) of all the waves of auditory brainstem response between the two groups (n=30)

Repetition rate	ABR Amplitude	Group	Mean(SD)	Inferential statistics
11.1/s	Wave I	Control	0.30(0.17)	U=345.0
	Wave I	Misophonia	0.34(0.13)	Z=1.54, p>0.05
	Wave III	Control	0.28(0.16)	U=374.0
	Wave III	Misophonia	0.31(0.11)	Z=1.12, p>0.05
	Wave V	Control	0.64(0.20)	U=397.0
	Wave V	Misophonia	0.57(0.21)	Z=0.77, p>0.05
90.1/s	Wave V	Control	0.47(0.16)	U=361.0
	Wave V	Misophonia	0.55(0.22)	Z=1.31, p>0.05

U; test statistics, Z score; standardized U statistic, p; significance value

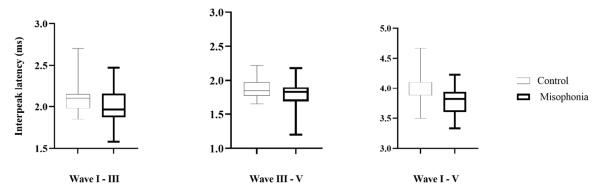


Figure 4. Median, quartiles, minimum, and maximum of interpeak latencies (ms) of all the auditory brainstem response waves at 11.1/s

U = 353.5

Z=1.43, p>0.05

U = 249.0

Z=2.97, p<0.05

11.1/s

auditory brainstem response between the two groups (n=30)						
Repetition rate	Interpeak latency	Group	Mean(SD)	Inferential statistics		
	Wave I-III	Control	2.09(0.15)	U=328.0		
	Wave I-III	Misophonia	2.02(0.21)	Z=1.80, p>0.05		

Control

Misophonia

Control

Misophonia

Table 4. The mean, standard deviation, and results of the Mann-Whitney U test for interpeak latencies (ms) of all the waves of auditory brainstem response between the two groups (n=30)

U; test statistics, Z score; standardized U statistic, p; significance value

Wave III-V

Wave III-V

Wave I-V

Wave I-V

individuals with misophonia [22]. Similarly, our study has also shown shortened latencies of ABR, which suggests heightened neural activity at the subcortical level in individuals with misophonia.

Interestingly, in the present study, no significant difference was observed in the absolute amplitude at lower and higher stimulus rates between the two groups, which underscores that while the timing of the neural response (latency) to sound is altered, the number of neurons firing (amplitude) response remains unaltered in individuals with misophonia. Similarly, a study by Aryal and Prabhu, also reported no significant difference in the amplitude of ABR that may be attributed to the inclusion of individuals with milder severity [21]. In contrast, Kim et al found that individuals with misophonia showed enhanced wave I amplitude compared to the control group [20]. Furthermore, the earlier interpeak latency of wave I-V in individuals with misophonia further supports the idea of a rapid neural response in this group, suggesting heightened activity of auditory signals through the brainstem. This is consistent with our study hypothesis that individuals with misophonia might process auditory stimuli more rapidly, contributing to the hypersensitivity characteristic of the condition. Thus, the results of our study provide objective evidence for hyperactivity at the sub-cortical level, resulting in faster conduction times as evidenced in ABR.

Consequently, this study provided valuable insights into the subtle differences in the auditory brainstem response findings among individuals with misophonia. Thus, the earlier arrival of auditory brainstem response waves could be a potential indicator in identifying misophonia, providing an electrophysiological index

to adjunct clinical assessments and enhancing our understanding of this condition. The study findings could help clinicians and researchers pave the way for tailored therapeutic interventions for individuals with misophonia.

1.87(0.14)

1.77(0.20)

3.96(0.22)

3.79(0.20)

Conclusion

The current study attempted to assess the auditory brainstem functioning of individuals with misophonia. The present study utilized electrophysiological measures and revealed that individuals with misophonia may exhibit heightened activity in the areas involved in generating Auditory Brainstem Response (ABR) waves III and V. Although ABR is sensitive to brainstem alterations, it is essential to note that auditory cortical and behavioral measures would supplement the ABR findings and provide a comprehensive understanding of the neurophysiological basis of misophonia. In our study, we recorded binaural ABR, suggesting that future research could explore and compare both monoaural and binaural ABR in individuals with misophonia. Additionally, the results need to be replicated in larger samples before considering ABR as a potential biomarker in individuals with higher severity of misophonia.

Ethical Considerations

Compliance with ethical guidelines

In the current study, all of the testing procedures were accomplished using a non-invasive technique and adhered to the conditions of the institutional ethical approval committee. The institutional ethical approval committee approved the current study AIISH Institute Review Board (IRB) Ref: SH/IRB/M.1/21/2024-25. The test procedures were clearly explained to the participants before testing. Written informed consent was taken prior to commencing the data collection.

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Authors' contributions

KK: Study design, acquisition of data, drafting the manuscript, interpretation of the results, critical revision of the manuscript, and statistical analysis; PP: Study design, supervision, drafting the manuscript, interpretation of the results, critical revision of the manuscript, and statistical analysis.

Conflict of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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