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Auditory brainstem functioning in individuals with misophonia

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A B S T R A C T

Purpose: Misophonia is not investigated much from an audiological perspective. Our study aims to examine the processing of the auditory retro-cochlear pathways in individuals with misophonia.
Methods: A cross-sectional study was conducted among university students who had misophonia. The revised Amsterdam Misophonia Scale was used to determine the severity of misophonia. Participants were divided into mild and moderate-severe misophonia and compared with the healthy control group. Auditory Brainstem Response testing was recorded from all the individuals with misophonia. The absolute latency, amplitude, inter-peak latency difference, and inter-rate latency difference were compared between the groups.
Results: One-way ANOVA result showed no significant difference in all the parameters of auditory brainstem response between the groups. These results are suggestive of normal brainstem processing in individuals with misophonia.
Conclusions: The study concludes that the auditory pathway up to brainstem areas is intact in individuals with misophonia. Further studies are essential on a larger population for generalizing the results.

1. Introduction

Misophonia is a disorder characterized by decreased sound tolerance to specific sound stimuli, known as triggers (Swedo et al., 2022). The triggers can be visual, auditory, or motor, and they may cause both emotional and physiological reactions, including anxiety, increased heart rate, sweating, rage, and irritation. The prevalence of misophonia is high, ranging from 23.28% (Aryal & Prabhu., 2022) to 49.1% (Naylor et al., 2021). Geographical region, variation in the sample, and methodology used could be the factors for variation in the prevalence rate.

Misophonia has not been categorized as a separate disorder by the Diagnostic and statistical manual (DSM-V) of mental disorders. This disorder borders neurology, physiology, and audiology (Danesh and Aazh., 2020), which can alter the physiological mechanism of the sufferers and result in distraction and annoyance. The lack of separate categorization hinders the recognition of the team members involved in the assessment and management of misophonia and hinders the sufferers from seeking help.

From the audiological perspective, less research is done to understand misophonia. Various researchers have shown abnormal activation of the cortical auditory structures in individuals with misophonia (Kumar et al., 2017, 2021; Grossini et al., 2022) through radiological investigations. In addition, studies have shown abnormal processing of the autonomic nervous system, including the limbic system, among misophonic (Kumar et al., 2017). However, no studies have reported abnormal neural processing of the retro-cochlear structures, including auditory nerve and brainstem structures, through radiological and audiological investigations. The pathophysiology of misophonia is not clear yet. However, various mechanism, origin, theories, and model has been explained in the literature to explain misophonia (Grossini et al., 2022; (Aryal & Prabhu., 2022). To understand misophonia from an audiological perspective, a new model has been developed which shows the linkage of misophonia with the classical and non-classical auditory pathway (Aryal & Prabhu., 2022).

Auditory evoked potentials (AEP) examine the auditory nerve fibers' synchronous discharge and detect abnormal neuronal activation. The waveform within the few 10 ms of the auditory evoked potentials is called auditory brainstem response (ABR). Auditory brainstem response (ABR) is the electrophysiological test that

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measures the neural activation of the auditory pathway from the dorsal auditory nerve to the inferior colliculus (Picton et al., 2000). Out of seven peaks of ABR, the first, third, and fifth peaks are clinically significant and arise from the dorsal part of the auditory nerve, cochlear nucleus, and lateral lemniscus, respectively (Picton and Durieux Smith., 1978). The shift in the latency of the Vth peak by greater than 0.8 s, when the rate increased from 11.1/sec to 90.1/sec, indicates retro cochlear pathology (Picton and Durieux Smith., 1978).

The primary aim of our study is to evaluate the processing of the retro-cochlear pathway in individuals with misophonia through electrophysiological tests. Abnormal ABR is reported among individuals with sound disorders such as tinnitus and hyperacusis (Sand and Saunte, 1994). Misophonia is a disorder that occurs in isolation or with other sound disorders such as tinnitus, hyperacusis, and phonophobia. We can hypothesize that abnormal neural processing up to the brainstem level might occur among individuals with misophonia due to its co-existence with these disorders. Hence, we aim to evaluate the peripheral retro-cochlear auditory pathway in individuals with misophonia by administering ABR testing. The present study was designed to determine whether significant differences exist in the ABR parameters in individuals with misophonia.

2. Methods

The All India Institute of Speech and Hearing institutional ethical review board reviewed the study protocol, and the ethical approval number was SH/ERB/2022-24/37. All the participants were informed about the study procedure before enrolling, and written informed consent was taken from all the participants.

2.1. Study participants

The cross-sectional study was conducted among individuals with clinically significant misophonia, and a comparison was made with the healthy control group. To find the prevalence and severity of misophonia, the survey was conducted among the students of Mysore University using the Revised Amsterdam misophonia questionnaire (Jager et al., 2020). The survey invited 30 individuals with misophonia symptoms to the study. All the participants were 18–40 years old, with a mean age of 25 years (SD = 7.8). Most participants, 36 (90%), were female, and 4 (10%) were male in the misophonia group. All participants had normal hearing sensitivity in the conventional pure-tone and high-frequency audiometry ranges. The control group consisted of 15 participants aged 20–40 years (Mean age = 24 years, SD = 6 years). The age and gender ratio was matched to the misophonia group. All the control group participants have normal audiograms in both conventional and high-frequency ranges. All the participants in the misophonia group had a history of misophonia for at least three years without any psychiatric and auditory disorders co-morbidities. In addition, only participants without any middle ear, cardiovascular, or neurologic illness, no history of acoustic trauma, and no ototoxic medication were included in both groups. Participants with hearing loss and other psychiatric and neurologic co-morbidities were excluded from the study.

2.2. Apparatus and procedure

A detailed physical examination was done, including case history, otoscopic examination, and general health examination. The revised Amsterdam misophonia questionnaire has been used to categorize misophonia into different severity ranges (Jager et al., 2020). The questionnaire has ten questions with a score ranging from 0 to 40. The score 0–10 are considered subclinical misophonia symptoms, the score of 11–20 are rated as mild misophonia, 21–30 as moderate to severe misophonia, and 31–40 as severe to extreme (Jager et al., 2020).

A hearing assessment was done using a Garson Stadler audio star pro using ANSI guidelines (Frank, 1997). The supraaural-49 headphone was used for the air conduction testing of the conventional pure tone audiometry, and the Radio-ear B-71 bone vibrator was used for the bone conduction testing. Similarly, Sennheiser circumaural HDA200 headphone was used for high-frequency audiometry. All the audiological tests were done in the soundproof room following the ANSI guidelines (Frank, 1997).

The frequencies from 250 Hz to 8 kHz were taken to determine the Air conduction threshold. Similarly, the frequencies from 250Hz to 4 kHz were taken for the bone conduction testing. The four frequency averages of 500Hz, 1 kHz, 2 kHz, and 4 kHz were taken to determine the threshold of each ear. As the criteria for normal hearing, an average air conduction value of 15 dB HL or less was taken (Olusanya et al., 2019). High-frequency audiometry was done for the frequencies from 9 kHz to 16 kHz. The six frequency average of 9 kHz, 10 kHz, 11.2 kHz, 12.5 kHz, 14 kHz, and 16 kHz was taken to determine the threshold.

Biologic Navigator Pro equipment was used to record auditory brainstem response (ABR) for all the participants. The recording was done in the soundproof room following the ANSI guidelines (Frank, 1997). The participants were instructed about the procedure and aim of the test before starting the recording. The participants were asked to sit in the reclining chair and ensure they were comfortable enough to begin the test. The participants were made ready for the test with proper cleaning, and they were instructed to sleep and relax during the entire testing to minimize the artifact and stabilize the electroencephalogram.

The single-channel recording was done in all the participants with vertical electrode montage. Test ear (A1 or A2) was used as the inverting electrode site (−), the Upper forehead (Fpz) was as the non-inverting electrode (+), and the contralateral ear of the test ear was used as the common ground electrode site using the 10–20 international electrode site classification (Homan et al., 1987). Cup electrodes were used for recording all the participants. Electrode Impedance of 3kΩ and inter-electrode impedance of 1kΩ was maintained during the entire recording for all the participants. To deliver the stimulus, Radio ear Insert-3A was used as the transducer. The click stimulus of 100-μs duration was used as the stimulus at the intensity of 90 dB SPL. The recording was done at two different rates, 11.1/s, and 90.1/s, with rarefaction polarity.

The acquisition parameters used were a filter setting of 100Hz–1500Hz, amplification of 1,00,000 times, a time window of 10 ms, and artifact rejection of 23.6 μV (Hurley, 2012). The averages of 1500 were taken, and consistency was maintained for all the participants included in the study. During the entire testing procedure, it was made sure that the electroencephalogram (EEG) was within the standard limit. The recording was done in all the participants with replication for reproducibility. The three experienced audiologists identified the peaks following the criteria established in the literature, with visualization of three sequences of the peaks as I-III-V using Bio-logic Auditory Evoked Potentials (Ver 7.2.1) software. The absolute latency, interpeak latency, inter-rate latency difference, and amplitude of ABR peak, i.e. I, III, and V were calculated and analyzed between the misophonia and control group.

The IBM SPSS program, version 25.0, was used for the data analysis. The Sapiro-Wilk test was carried out to determine the normality. As the data followed a normal distribution, a parametric one-way ANOVA test was conducted to find the significant differences between the misophonia and control groups. The dependent variables were the latency and amplitude of all the peaks, and the independent variable was the severity of misophonia. The criteria for statistical significance was set at a p-value of less than 0.05 with a 95% confidence interval.

3. Results

3.1. Misophonia severity

We found that 10 participants had moderate to severe misophonia with scores ranging from 21 to 30, 5 participants had severe to extreme misophonia with a score ranging from 31 to 40, and 15 participants had mild misophonia with a score ranging from 11 to 20. Altogether, 30 participants were included in the misophonia group. All 15 participants who were included as the control group had a score of zero on the revised RAMISO-S scale. We did not have enough data for the misophonia group to form the three groups; hence, we divided participants into two groups, one mild misophonia group and another moderate-severe misophonia group. The mild misophonia group had a score of 15.93 (SD = 2.89), and the moderate-severe misophonia group (N = 15) with a mean score of 25.86 (SD = 4.98). All the participants included in the study had misophonia for 4.9 years with a variation from 3 to 8 years (Mean = 4.93, SD = 1.52).

3.2. Audiological evaluation

The physical examination showed a normal appearance of the external and middle ear in all the participants. All the participants had normal health conditions with normal hearing. The result did not show a statistically significant difference in the air conduction threshold between the study and control groups with (F (2.42) = 0.587, p = 0.561) for the right ear and with (F (2.42) = 2.540, p = 0.091) for the left ear. Similarly, we did not find statistically significant differences between the study and control groups for the bone conduction threshold also, with (F (2.42) = 0.678, p = 0.66) for the right ear and with (F (2.42) = 1.540, p = 0.08) for the left ear as illustrated in Table 1.

The results of the high-frequency audiometry showed the presence of normal hearing in the high-frequency range from 9 kHz to 16 kHz for all the participants. The ANOVA result did not show any significant difference in the mean high-frequency average between the groups, with (F (2.42) = 3.401, p = 0.062) for the right ear and with (F (2.42) = 1.769, p = 0.183) for the left ear. Table 1 shows the audiological findings of pure-tone and high-frequency audiometry.

3.3. Auditory brainstem response (ABR) findings

The result of the Auditory Brainstem Response (ABR) was analyzed to determine the neural processing in the retro-cochlear pathway. During the entire recording, electrode impendence was less than 3kΩ, and the inter-electrode difference was less than 1kΩ (Hurley, 2012). The absolute latency, the amplitude of all the peaks, interpeak latency, and latency difference at the different rate was analyzed for all the participants.

3.3.1. Absolute latency

Absolute latency of I, III, and Vth peaks was analyzed between the groups at two different rates: 11.1/sec and 90.1/sec. For the rate of 11.1/sec, the result of the one-way ANOVA showed no significant differences between the group for the absolute latency values of the I peak, III peak, and V peak for both ears (p > 0.05). Similarly, for the rate of 90.1/sec, we did not find a significant difference between the groups for the absolute latency values of the I peak, III peak, and V peak for both ears p > 0.05). The mean and standard deviation of all the peaks of ABR, along with the one-way ANOVA result, are illustrated in Table 2 and Table 3 for the right ear and left ear, respectively.

3.3.2. Amplitude of peaks

The amplitude of all the peaks of ABR was analyzed between the groups. The rate used was 11.1/s. The mean value and standard deviation of all the peaks of ABR are illustrated in Figs. 1 and 2, respectively.

The result of the one-way ANOVA showed no significant differences in the amplitude of all the peaks for both ears. For the amplitude of the I peak, no significant difference was found between the groups with (F (2.42) = 1.62, p = 0.21) for the right ear and (F (2.42) = 1.52, p = 0.31) for the left ear. Similarly, for the amplitude of the III peak, we did not find any significant difference between the groups with (F (2.42) = 1.19, p = 0.32) for the right ear and (F (2.42) = 1.52, p = 0.31) for the left ear. For the Vth peak also, no significant differences were found between the groups with (F (2.42) = 0.31, p = 0.74) for the right ear and (F (2.42) = 0.35, p = 0.71) for the left ear.

Table 1
Result of the pure tone audiometry and high frequency audiometry between the groups for the Right ear and left ear (N = 45).

GROUP		HEARING THRESHOLD					
		Pure tone average (dBHL)				High frequency average (dB SPL)	
		Right ear		Left ear		Right ear	Left ear
		Air conduction	Bone Conduction	Air Conduction	Bone Conduction		
CONTROL	Mean	6.08	3.5	7.75	4.8	7.47	8.36
	N	15	15	15	15	15	15
	Std. Deviation	3.07	1.7	3.69	2.2	2.57	4.16
MILD	Mean	7.75	3.2	6.08	4.5	8.33	10.72
	N	15	15	15	15	15	15
	Std. Deviation	7.58	2.5	4.60	1.5	3.34	5.16
MODERATE-SEVERE	Mean	8.33	4	7.75	4.5	8.43	11.28
	N	15	15	15	15	15	15
	Std. Deviation	6.58	1.7	3.69	2.2	3.05	4.09
F-value		**0.59**	**0.68**	**2.54**	**1.54**	**3.40**	**1.77**
Sig.		**0.56**	**0.66**	**0.09**	**0.08**	**0.06**	**0.18**

Table 2
Result of one-way ANOVA showing the absolute latency of I, III, and Vth peaks at two different rates (11.1/s and 90.1/s) for the right ear.

GROUP		ABSOLUTE LATENCY (ms)					
		11.1/sec			90.1/sec		
		I	III	V	I	III	V
CONTROL	Mean	1.44	3.48	5.08	1.56	3.69	5.66
	N	15	15	15	15	15	15
	Std. Deviation	0.19	0.16	0.37	0.24	0.16	0.27
MILD	Mean	1.36	3.56	5.15	1.56	3.65	5.62
	N	15	15	15	15	15	15
	Std. Deviation	0.12	0.49	0.19	0.23	0.36	0.20
MODERATE-SEVERE	Mean	1.43	3.55	5.22	1.46	3.81	5.66
	N	15	15	15	15	15	15
	Std. Deviation	0.12	0.15	0.27	0.43	0.19	0.28
F-value		**1.37**	**0.90**	**0.95**	**0.48**	**1.71**	**0.13**
Sig.		**0.26**	**0.41**	**0.39**	**0.62**	**1.93**	**0.88**

Table 3
Result of one-way ANOVA showing the absolute latency of I, III, and Vth peaks at two different rates (11.1/s and 90.1/s) for the left ear.

GROUP		ABSOLUTE LATENCY (ms)					
		11.1/sec			90.1/sec		
		I	III	V	I	III	V
CONTROL	Mean	1.50	3.54	5.13	1.53	3.78	5.71
	N	15	15	15	15	15	15
	Std. Deviation	0.14	0.12	0.29	0.45	0.17	0.22
MILD	Mean	1.37	3.58	5.25	1.49	3.59	5.72
	N	15	15	15	15	15	15
	Std. Deviation	0.39	0.19	0.22	0.63	0.86	0.14
MODERATE-SEVERE	Mean	1.47	3.61	5.31	1.66	3.95	5.79
	N	15	15	15	15	15	15
	Std. Deviation	0.08	0.16	0.29	0.14	0.23	0.26
F-value		**1.06**	**0.66**	**1.62**	**0.55**	**1.31**	**0.69**
Sig.		**0.36**	**0.52**	**0.21**	**0.58**	**0.28**	**0.51**

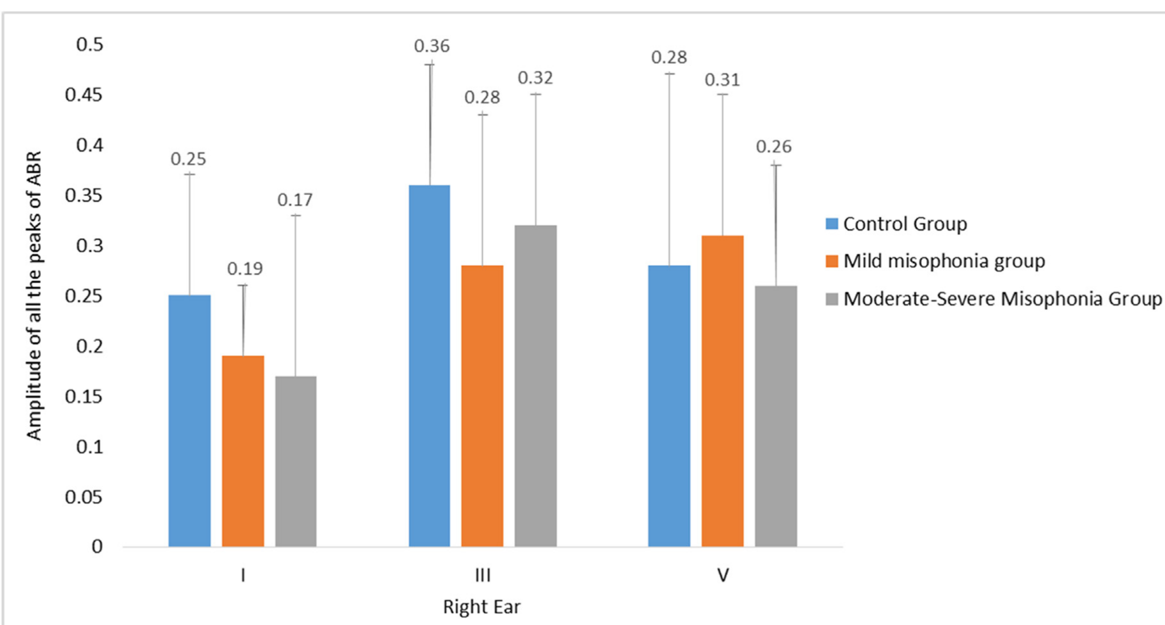

Fig. 1. Representation of amplitude of all the peaks of ABR for the Right ear (N = 45).

3.3.3. *Interpeak latency (IPL)*

Interpeak latency difference of I and III peaks, III and Vth peak, and I and Vth peak were analyzed at the rate of 11.1/s between the control group and the misophonia group. The result of the one-way ANOVA showed no significant difference between the groups for all the interpeak latency differences ($p > 0.05$) as illustrated in Table 4.

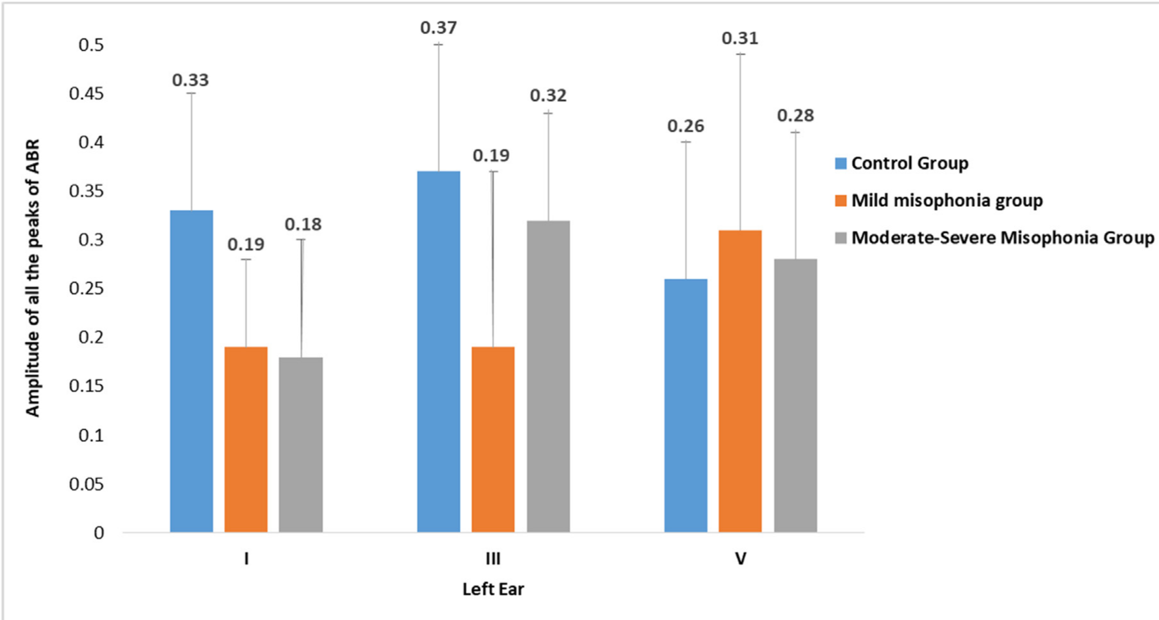

Fig. 2. Representation of amplitude of all the peaks of ABR for the left ear (N = 45).

Table 4
Result of one-way ANOVA showing Interpeak latency difference between the groups for the Right ear and Left ear at the rate of 11.1/s.

GROUP		INTER-PEAK LATENCY DIFFERENCE (ms)					
		RIGHT EAR			LEFT EAR		
		I-III	III-V	I–V	I-III	III-V	I–V
CONTROL	Mean	2.04	1.59	3.64	2.05	1.59	3.63
	N	15	15	15	15	15	15
	Std. Deviation	0.14	0.35	0.30	0.13	0.30	0.27
MILD	Mean	2.20	1.60	3.80	2.00	1.67	3.49
	N	15	15	15	15	15	15
	Std. Deviation	0.22	0.21	0.21	0.57	0.33	0.98
MODERATE-SEVERE	Mean	2.12	1.67	3.64	2.14	1.69	3.83
	N	15	15	15	15	15	15
	Std. Deviation	0.16	0.25	0.66	0.17	0.23	0.29
F-value		**3.18**	**0.36**	**0.71**	**0.65**	**0.57**	**1.19**
Sig.		**0.05**	**0.70**	**0.49**	**0.53**	**0.57**	**0.32**

3.3.4. Inter-rate latency difference

The absolute latency difference at two rates: 11.1/s and 90.1/s, was calculated by subtracting the absolute latency value at 11.1/sec from 90.1/sec. The comparison was made between the two misophonia groups and the control group. The mean value of absolute latency difference at two different rates (11.1/s and 90.1/s) was found to be less than 0.8ms suggesting no indication of retrocochlear pathology. The mean and standard deviation value for rate differences values for all the peaks along the ANOVA result is illustrated in Table 5. The result of the one-way ANOVA showed no significant difference in the rate difference values for all the peaks ($p > 0.05$), as illustrated in Table 5.

4. Discussion

Our study aimed to analyze the processing of the brainstem pathway in individuals with misophonia through auditory brainstem response (ABR) testing. The ABR was performed on all the participants, and responses were analyzed between the control and misophonia groups. The absolute latency of the peaks, amplitude, interpeak latency differences, and inter-rate latency differences was calculated and analyzed among all the participants recruited in the study. The comparison of the ABR parameters of the misophonia group with the control group showed no significant differences in all the ABR parameters. These results showed the presence of normal retro-cochlear pathway processing up to the brainstem structures among individuals with misophonia.

Misophonia is a disorder that may occur alone or in association with other auditory disorders, such as tinnitus and hyperacusis (Dozier, 2015). There has been growing interest in the use of ABR among individuals with tinnitus. Various studies have shown an increase in latency and a decrease in amplitude of all the peaks of ABR among individuals with tinnitus (Sand and Saunte., 1994; Keith and Greville, 1987). As misophonia occurs in association with these auditory disorders, we hypothesized that there could be some differences in neural processing at the level of the peripheral nervous system among individuals with misophonia. However, the result of our study showed no significant differences in the ABR parameters among individuals with misophonia, rejecting the hypothesis. The difference in these findings among tinnitus and misophonia showed a difference in pathophysiology among these disorders. However, this is the first study of this kind among

Table 5
Result of ANOVA showing absolute latency difference at two different rate (11.1/s and 90.1/s) between the groups for the Right ear and left ear (N = 45).

GROUP		INTER-RATE ABSOLUTE LATENCY DIFFERENCE (90.1/S-11.1/s)					
		RIGHT EAR			LEFT EAR		
		I	III	V	I	III	V
CONTROL	Mean	0.14	0.20	0.58	0.14	0.24	0.58
	N	15	15	15	15	15	15
	Std. Deviation	0.11	0.08	0.26	0.15	0.11	0.29
MILD	Mean	0.24	0.23	0.44	0.22	0.25	0.46
	N	15	15	15	15	15	15
	Std. Deviation	0.23	0.16	0.22	0.15	0.17	0.23
MODERATE-SEVERE	Mean	0.16	0.28	0.44	0.19	0.34	0.49
	N	15	15	15	15	15	15
	Std. Deviation	0.14	0.16	0.17	0.15	0.13	0.30
F-value		**1.45**	**1.69**	**2.03**	**1.17**	**2.09**	**0.74**
Sig.		**0.25**	**0.19**	**0.15**	**0.32**	**0.14**	**0.49**

misophonia and needs to replicate the findings in the future, taking a larger sample size.

Various neuroimaging investigations using functional magnetic resonance imaging (fMRI) has shown abnormal processing of the various auditory cortical areas, including non-classical auditory pathway among individuals with misophonia (Kumar et al., 2017; Brout et al., 2018). However, no neuroimaging studies have reported abnormal processing of sub-cortical auditory pathways, including brainstem areas, among individuals with misophonia. Our study also supports neuroimaging studies' findings, suggesting normal processing of retrocochlear structures among individuals with misophonia. These findings from the electrophysiological and neuroimaging investigation suggest retro-cochlear structure abnormalities are absent among individuals with misophonia.

In our study, we assessed the ABR using both low and high stimulation rates. Both rate levels did not show any significant difference in the ABR findings among the control and misophonia groups. These results suggest the presence of normal neural synchrony up to brainstem areas among individuals with misophonia. However, our study could not obtain frequency-specific ABR responses as we used the click stimulus (Robier et al., 1992). Hence, there is a need to carry out studies in the future using frequency-specific stimuli.

5. Conclusion

Our study concludes normal processing of the retro-cochlear pathway among individuals with misophonia. However, this is the first study of this kind, and further studies on the larger population are needed to generalize the results. The result of our research would be the baseline for all the neurologists, audiologists, and psychologists working in misophonia to understand the disorder.

5.1. Limitations and future directions

There is a shortage of studies in the literature assessing misophonia from the audiological perspective. Our study showed normal auditory brainstem responses in individuals with misophonia. The result of our research using the electrophysiological measure supports the findings of the functional Magnetic Resonance Imaging (fMRI) studies reported in the literature. However, this is the first study of this kind from the audiological perspective. We need to validate our findings in the future, taking a larger sample size. In addition, we need to carry out studies in the future using frequency-specific stimuli. Furthermore, our study used the most widely used questionnaire RAMISO-S for assessing misophonia and its severity, which is unavailable in the native Indian language and population. There is a need to carry out the study in the future, using the questionnaire standardized in the native language.

Authors' contribution

Sajana Aryal was involved in concept development, study design, stimulus preparation, analysis of the results, interpretation, and writing the manuscript**; Prashanth Prabhu** was involved in concept development and study design, stimulus preparation, and writing the manuscript.

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Declaration of competing interest

There is no conflict of interest to disclose.

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