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NO AFTER-EFFECTS OF COVID-19 INFECTION IN TERMS OF STANDARD AUDIOLOGICAL TESTS

Contributions:
A Study design/planning
B Data collection/entry
C Data analysis/statistics
D Data interpretation
E Preparation of manuscript
F Literature analysis/search
G Funds collection

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Abstract

Introduction: Coronavirus disease (COVID-19), considered to be caused by a novel coronavirus (SARS-CoV-2), is an acute respiratory disease which was declared a pandemic by the World Health Organization. Previously published reports have shown contradictory findings on the involvement of the auditory system in individuals infected with COVID-19. The present study aims to assess auditory system functioning in individuals post-COVID-19 infection and compare the results with individuals without COVID-19 infection.

Material and methods: Participants in this study were 30 individuals who had experienced mild COVID-19 infection and 30 individuals who never had COVID-19. Participants were aged between 18 and 40 years. Testing was done 1 to 6 months after infection, and involved conventional and extended high-frequency audiometry, speech perception in quiet and at different signal-to-noise ratios (SPIN), transient evoked otoacoustic emissions (TEOAEs) in quiet and in the presence of contralateral noise, and auditory brainstem response (ABR) in the ipsilateral and contralateral mode.

Results: None of the tests – pure-tone thresholds, speech perception in quiet and in noise, TEOAE with and without contralateral noise, and ABR – showed any significant difference between individuals who never had COVID-19 infection and those who had recovered from the infection. Both afferent and efferent auditory pathways showed normal findings in individuals post-COVID-19 infection.

Conclusions: Individuals who have been infected with mild COVID-19 did not show any significant deficit in any of the audiological tests, suggesting that the disease does not cause any permanent harm to the auditory system after the infection has subsided.

Key words: COVID-19 • auditory brainstem response • pure-tone thresholds • otoacoustic emission • speech-in-noise

BRAK NASTĘPSTW INFEKCJI COVID-19 W ODNIESIENIU DO STANDARDOWYCH TESTÓW AUDIOLOGICZNYCH

Streszczenie

Wprowadzenie: Choroba COVID-19, uważana za powodowaną przez nowy koronawirus (SARS-CoV-2), to ostre zakażenie układu oddechowego uznane przez Światową Organizację Zdrowia za pandemię. Wcześniej publikowane artykuły raportowały sprzeczne wyniki odnośnie wpływu choroby COVID-19 na układ słuchowy u osób zakażonych. Prezentowane badanie miało na celu ocenę funkcjonowania układu słuchowego u osób, które przebyły infekcję wirusem COVID-19, i porównanie tych wyników z wynikami uzyskanymi u osób, które nie były zakażone COVID-19.

Materiał i metody: W badaniu uczestniczyło 30 osób, które przeszły łagodne zakażenie COVID-19, oraz 30 osób, które nie chorowały na COVID-19. Wiek uczestników wynosił między 18 a 40 lat. Testy wykonane po upływie 1 do 6 miesięcy od zakażenia obejmowały: audiometrię konwencjonalną i wysokoczęstotliwościową, badanie percepcji mowy w ciszy i przy różnych stosunkach sygnału do szumu (SPIN), badanie emisji otoakustycznych wywołanych trzaskiem (TEOAE) w ciszy i w obecności szumu w drugim uchu oraz badanie słuchowych potencjałów wywołanych pnia mózgu (ABR) w układzie ipsilateralnym i kontralateralnym.

Wyniki: W żadnym z przeprowadzonych badań – audiometrii tonalnej, percepcji mowy w ciszy i w szumie, TEOAE z i bez kontralateralnego szumu oraz ABR – nie uzyskano istotnej różnicy wyników między osobami, które nigdy nie chorowały na COVID-19, a tymi, które wyzdrowiały po zakażeniu. Wyniki otrzymane zarówno z dośrodkowej, jak i odśrodkowej ścieżki słuchowej u osób po zakażeniu COVID-19 mieściły się w normie.

Wnioski: Osoby, które przeszły łagodne zakażenie COVID-19 nie wykazywały istotnego deficytu w żadnym z testów audiologicznych, co sugeruje, że choroba ta nie powoduje żadnych stałych uszkodzeń układu słuchowego po ustąpieniu zakażenia.

Słowa kluczowe: COVID-19 • słuchowe potencjały wywołane pnia mózgu • audiometria tonalna • emisje otoakustyczne • percepcja mowy w warunkach szumu otoczenia

Introduction

Coronavirus disease (COVID-19) is caused by a novel coronavirus (SARS-CoV-2), and is an acute respiratory disease which was declared a pandemic on 30 January 2020 by the World Health Organization (WHO). According to Government of India statistics, the total number of individuals in the country infected with COVID-19 was 43,452,164 as of 30 June 2022. Of this number, 42,822,493 were cured and 104,555 were still infected and undergoing treatment [1]. Common symptoms of COVID-19 include fever, mild to moderate respiratory illness, fatigue, and gastrointestinal complaints [2]. Older adults and those with other health problems are more prone to the disease, and infection may lead to severe consequences. Individuals with the infection who show significant symptoms are referred to as symptomatic patients while others may not show any symptoms even though they are infected with the virus and can act as a carrier. The majority of individuals recover well with minimal medical support, although a small proportion suffer severe respiratory distress which if not treated may be fatal.

Many viral infections – such as mumps, measles, and meningitis – can cause significant hearing loss. Since COVID-19 is also caused by a virus (SARS-CoV-2), it is important to check whether there is any association between COVID-19 infection and subsequent hearing loss. In particular, it is important to monitor the hearing status of individuals after COVID-19 infection, as so many individuals have been infected with the virus. If hearing loss is not detected soon after the infection, rehabilitation costs may escalate. It is also important to investigate the nature of the hearing loss from COVID-19 – whether it is permanent or temporary, and whether stable or progressive. There has also been a report of neuronal degeneration in individuals with SARS-CoV-2 [3]. Mao et al. reported nonspecific neurological symptoms such as dizziness, ataxia, and neuralgia due to involvement of the cranial nerve. This means there could be damage to the afferent and efferent pathways of the vestibulocochlear nerve, and this aspect also needs investigation. One audiological test to assess the integrity of the efferent pathways of the auditory system is to record otoacoustic emissions (OAEs) in the presence of contralateral noise. At the same time, auditory brainstem responses (ABRs) can be used to assess the integrity of the afferent auditory pathway.

Several studies have highlighted the effect of COVID-19 infection on the functioning of the auditory system, but the results so far have not been consistent [2,4–9]. The present study aims to assess the auditory system functioning in individuals post-COVID-19 infection and to compare the results from individuals who have not been infected.

Material and methods

For the study we recruited 30 individuals without a history of COVID-19 infection and 30 individuals with a history of COVID-19 infection. The age range of participants in both groups was 18 years to 40 years (mean ages 27.5 and 28.3 years respectively). Inclusion criteria for individuals with COVID-19 was to have a positive reverse transcription polymerase chain reaction (RT-PCR) test confirming the infection and a subsequent negative RT-PCR test confirming recovery. Individuals with only mild COVID-19 illness were considered for the study [10]. Mild illness was defined as signs and symptoms of COVID-19 including fever, cough, sore throat, headache, muscle pain, nausea, vomiting, diarrhea, and loss of taste and smell, but excluded symptoms such as shortness of breath, dyspnea, or abnormal chest imaging [10].

The audiological testing for individuals with COVID-19 was done 1 to 6 months after being infected. Patients were not considered less than 1 month after infection, as they might still have conductive hearing loss due to throat infection, one of the major symptoms of COVID-19. Excluded from the study were individuals with significant hearing loss before the infection, patients less than 18 or more than 50 years of age, and patients with other medical conditions such as diabetes, hypertension, heart problems, chronic ear infection, intake of ototoxic medication. Similarly, patients who suffered severe COVID-19 symptoms and required hospitalisation for more than a week, and those who were admitted to an intensive care unit, were excluded from the study. The individuals without COVID-19 were those who have never had any COVID-19-related symptoms in the past year as per the classification suggested by the National Institutes of Health [10]. The present study was approved by the institutional ethics committee; written informed consent was obtained from all participants before administering the tests.

The audiological evaluation comprised conventional pure-tone audiometry, extended high-frequency audiometry, transient evoked otoacoustic emissions (TEOAEs) with and without contralateral noise, auditory brainstem responses (ABRs) in ipsilateral and contralateral mode, and speech perception in quiet and in the presence of noise. Both the afferent and efferent pathways were assessed: the afferent pathway was assessed using ABR and the efferent pathway was assessed using a contralateral recording of ABR and contralateral suppression of TEOAEs. All the audiological evaluations were done in a sound-treated room with ambient noise levels within permissible limits.

Conventional pure-tone audiometry and extended high-frequency audiometry

All participants' air conduction thresholds were measured from 0.25 to 8 kHz (conventional pure-tone audiometry) and from 9 to 14 kHz (extended high-frequency audiometry) using a calibrated two-channel diagnostic Piano Inventis audiometer (Investis SRL, Corso StatiUniti, Padova, Italy) and Sennheiser HDA 200 headphones. Bone conduction thresholds were obtained from 0.25 to 4 kHz using a Radio Ear B71 bone vibrator. Audiometric thresholds were estimated using the modified Hughson–Westlake procedure [11]. Clark's classification of hearing loss was used to diagnose the degree of loss [12]. Both ears of all participants were evaluated.

Tympanometry

Tympanometry was carried out to rule out any middle ear pathology that might result in elevated pure-tone thresholds and absent OAE responses. A calibrated middle ear

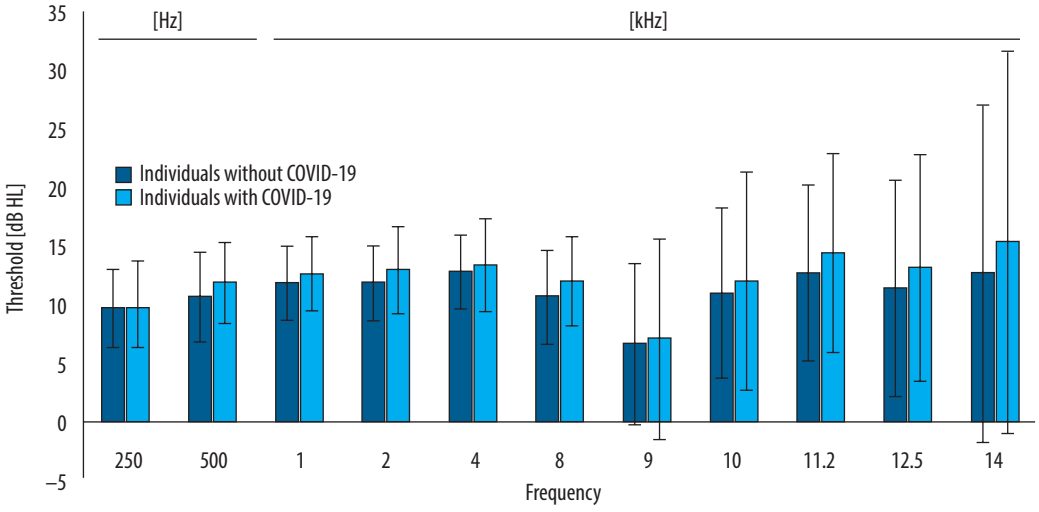

Figure 1. Means and standard deviations of thresholds obtained from individuals with and without COVID-19

analyser (Interacoustics AT-235) was used for tympanometry, with a 226 Hz probe tone. All the participants who had an 'A' type of tympanogram were selected for the study [13].

TEOAEs with and without contralateral noise

TEOAEs were used to assess the functioning of the outer hair cells of the inner ear. A calibrated Otodynamics Ltd EZ screen otoacoustic emission system was used for testing TEOAEs and their suppression. Participants sat comfortably in a chair in a soundproof room and were instructed to relax and breathe normally to minimise breathing noise. Both the ears of all participants were evaluated. First, the TEOAE responses were recorded without noise, and then a second recording was done with contralateral noise. Nonlinear click stimuli of 80 dB peak sound pressure level (SPL) were delivered to the ear canal. Each trial used a total of 260 averages. The frequencies tested were 1, 1.5, 2, 3, and 4 kHz. The response parameters were a reproducibility of > 70%, response stability of > 80%, and signal-to-noise ratio > 6 dB. To study the contralateral suppression of TEOAEs, target stimuli of 80 dB peak SPL were given to the test ear, and 50 dB SPL of white noise was provided to the contralateral ear using an insert earphone connected to a calibrated audiometer [5]. These levels of target stimuli and contralateral noise were used to elicit good amplitude TEOAEs and obvious contralateral suppression [14] while ensuring that the stimuli were below the level to elicit middle-ear muscle reflex. The signal-to-noise ratios (SNRs) of the TEOAE responses were recorded. A reduction in TEOAE response with the addition of contralateral noise was considered to show the presence of TEOAE suppression.

Auditory brainstem response

ABRs were recorded in both ipsilateral and contralateral mode using a dual channel SmartEP from Intelligent Hearing Systems. Recording of ABR in the ipsilateral mode gives information about the afferent auditory pathway and ABR recording in the contralateral mode assesses the efferent pathway. ABRs were recorded using 100 ms clicks at rates of 11.1/s and 90.1/s. The non-inverting electrode was placed on Fz, while inverting electrodes were placed on both mastoids and the ground electrode on the forehead. Two blocks of 1500 sweeps were recorded from each participant. The I, III, and V peaks were marked for both repetition rates for ipsilateral and contralateral recording. Both ears of all participants were evaluated.

Speech perception in quiet and in the presence of noise

Speech perception was assessed using 10 words and 6 sentences with high-frequency composition [15]. Stimuli were standardised high-frequency words and sentences developed at the All India Institute of Speech and Hearing, Mysuru, Karnataka, India. Speech perception was assessed in quiet and at different signal-to-noise ratios (SNRs of +3 dB, 0 dB, –3 dB, –6 dB). The stimuli were mixed with speech noise using Adobe Audition software. The stimuli were presented at 60 dB SPL binaurally through a laptop routed through a calibrated audiometer. The participants were asked to repeat the words and sentences as accurately as possible. The presentation order of the SNRs was randomised across individuals.

IBM SPSS Statistics (version 23) software was used to analyse data obtained from pure-tone audiometry, extended high-frequency audiometry, TEOAEs with and without contralateral noise, ABR, and speech perception in quiet and at different SNRs.

Results

Shapiro–Wilk tests of normality showed data obtained from both groups to be non-normally distributed ($p < 0.05$) and thus non-parametric statistics were used. A Wilcoxon signed-rank test was used to compare the responses obtained from the right and left ears. The result showed no significant difference in values between the right and left ears for pure-tone audiometry, TEOAEs, and ABRs. Thus the data from both ears were combined, giving 60 ears in

Table 1. Means and standard deviations of TEOAE responses for individuals with and without COVID-19

Groups	Frequency [kHz]	Without contralateral noise		With contralateral noise		Amount of suppression
		Mean	*SD*	Mean	*SD*	
Individuals without COVID-19	1	16.93	7.91	17.26	7.90	–0.33
	1.5	22.01	6.16	21.40	6.47	0.61
	2	21.34	5.30	20.75	5.86	0.59
	3	18.97	5.58	18.70	5.50	0.27
	4	15.09	5.46	15.49	5.31	–0.40
Individuals with COVID-19	1	16.40	6.37	15.51	5.59	0.89
	1.5	20.68	6.50	18.96	8.05	1.72
	2	19.81	5.72	18.84	6.16	0.97
	3	18.11	5.70	17.70	5.58	0.41
	4	15.11	6.54	14.94	7.23	0.17

Table 2. Comparison of TEOAE responses obtained from individuals without and with COVID-19

Frequency [kHz]	Without contralateral noise		With contralateral noise	
	Z-value	*p*-value	*Z*-value	*p*-value
1	0.58	0.55	–1.37	0.16
1.5	–1.18	0.23	–1.66	0.09
2	–1.50	0.13	–2.08	0.06
3	–1.49	0.13	–2.18	0.12
4	–0.65	0.51	–0.80	0.42

each group. A Mann–Whitney *U*-test was done to compare the data obtained from individuals with and without COVID-19. A Wilcoxon signed-rank test was done for within-group comparison of the speech scores.

Conventional pure-tone audiometry and extended high-frequency audiometry

The means and standard deviations for the thresholds obtained from both groups are shown in **Figure 1**. As can be seen, the hearing thresholds were well within the normal range across all frequencies. The Mann–Whitney *U*-test results showed no significant difference in hearing thresholds from 0.25 to 14 kHz between both the groups of individuals with and without COVID-19 ($p > 0.05$).

TEOAEs without and with contralateral noise

Table 1 shows the means and standard deviations of the TEOAE responses obtained from individuals with and without COVID-19 infection; the table also shows the amount of response suppression. For both groups of participants there was a reduction in TEOAE responses with the addition of noise. The Mann–Whitney *U*-test values for the TEOAE responses are given in **Table 2**. TEOAE responses with and without contralateral noise showed no statistically significant difference between the individuals with and without COVID-19.

Auditory brainstem response

The latency and amplitude values of ABR peaks for the ipsilateral and contralateral recordings are shown in **Figure 2**. The ABR latency and amplitude values of all the peaks showed no statistically significant difference between the groups of individuals with and without COVID-19. The responses from individuals with COVID-19 followed a normal trend.

Speech perception in quiet and in the presence of noise

Table 3 shows the speech perception scores obtained for high-frequency words and sentences at different SNRs for individuals with and without COVID-19. Mann–Whitney *U*-test results showed no significant difference between the scores of individuals with and without COVID-19 for quiet conditions and for any of the SNRs as shown in **Table 4**. Both groups performed similarly, with better performance at +3 dB, 0 dB, and in quiet, but performance deteriorated with negative SNRs.

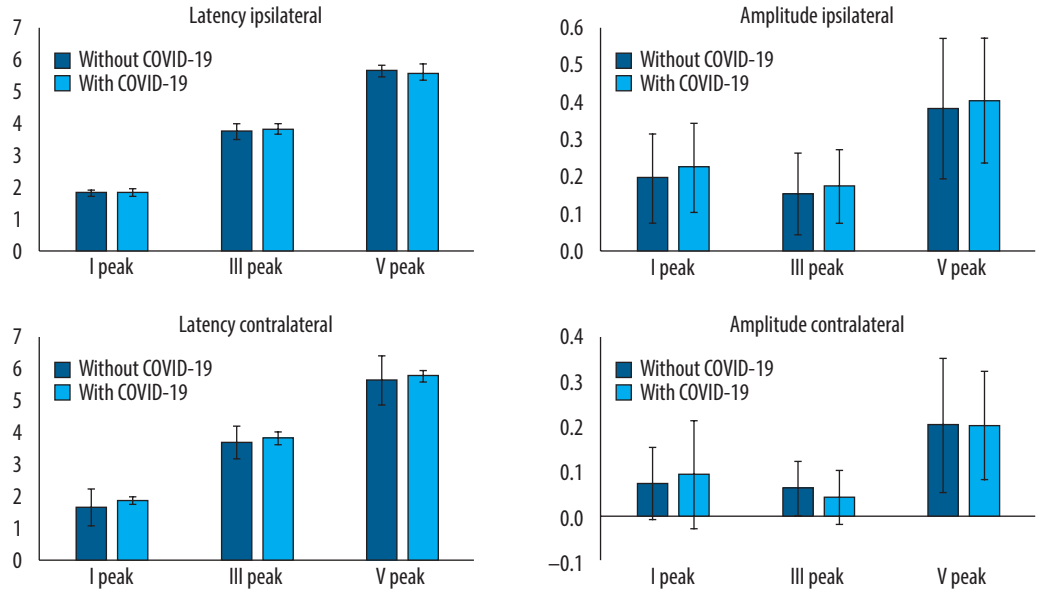

Figure 2. Latency [ms] and amplitude [μV] of ABR peaks for the ipsilateral and the contralateral responses of individuals with and without COVID-19

Table 3. Speech scores obtained for high-frequency words and sentences from individuals with and without COVID-19

Condition	Individuals without COVID-19		Individuals with COVID-19	
	words	sentences	words	sentences
–6 dB SNR	8	4	8	4
–3 dB SNR	9	5	8	5
0 dB SNR	10	5	10	5
+3 dB SNR	10	5	10	5
Quiet	10	5	10	5

Table 4. Comparison of scores obtained for individuals with and without COVID-19 infection for words and sentences at different SNRs

Condition	Words		Sentences	
	Z-value	*p*-value	*Z*-value	*p*-value
–6 dB SNR	–0.86	0.38	–1.85	0.06
–3 dB SNR	–1.09	0.27	–1.21	0.22
0 dB SNR	–1.40	0.16	–1.00	0.31
+3 dB SNR	–0.38	0.70	0.00	1.00
Quiet	–1.00	0.31	0.00	1.00

Discussion

COVID-19 is a viral infection that started in 2019 and has since covered the entire globe in just 3 years. Its manifestations are changing with time, and infected individuals show a gamut of symptoms ranging from fever, mild to moderate respiratory illness, fatigue, and gastrointestinal complaints [2,16]. Individuals with COVID-19 can have long-term complications, including lung damage, neurological disorders, and heart disorders. Recent studies also point to hearing loss as one of the possible complications. Some have demonstrated a negative effect of COVID-19 on hearing function tests [5,9,17–22] while others have shown, in patients who have recovered from mild-to-moderate degrees of infection, no significant difference before and after COVID-19 infection [6–8,23]. In 2020 Mustafa reported significantly reduced high-frequency pure-tone thresholds and reduced otoacoustic emission (OAE) amplitude in

asymptomatic COVID-19 patients [2]. Meanwhile, Gallus et al. reported audiovestibular system dysfunction in a significant number of individuals post-COVID-19 infection: 8.3% reported subjective hearing loss, 4.2% reported tinnitus, 8.3% reported dizziness, 2% reported vertigo, 2% dynamic imbalance, and 6.3% showed static imbalance. Pure-tone audiometry and video head impulse tests were normal for all individuals post-COVID-19 [16].

In the present study, pure-tone thresholds of individuals in both groups, and for conventional and extended high frequencies, showed similar audiometric thresholds, suggesting no significant effect of COVID-19 infection on hearing sensitivity. There are several reports highlighting the negative effects of COVID-19 infection on hearing. Kilic and colleagues were the first to suggest hearing loss as one of the consequences of COVID-19 infection [6]. Other researchers have also reported hearing-related symptoms in individuals with COVID-19 infection [16,25,26]. High-frequency hearing loss and the absence of TEOAEs have been observed in a number of individuals post-COVID-19 infection [2,5].

The above studies indicate abnormal responses of the ear to sounds. There can be several possible reasons. Most of the studies cited have included individuals with comorbid conditions such as diabetes and hypertension. These comorbid disorders can themselves result in the deterioration of hearing thresholds [20,27,28]. However, in the present study participants with comorbid conditions were excluded, which might be one of the reasons for our normal audiological findings post-COVID-19. A second reason for seeing no hearing impairment in individuals infected with COVID-19 in the present study could be the age of the population – i.e. 18 to 40 years of age. A few studies have reported hearing loss in individuals with COVID-19 who are more than 50 years old [20]. Wang and colleagues reported deterioration in extended high-frequency audiometry in healthy adults with normal hearing in different age groups, but it was most obvious in the older age group – i.e. 51–60 years of age. Further, the effect of age on hearing acuity was evident in conventional audiometry at frequencies above 4 kHz [29]. Apart from COVID-19 infection, age-related hearing loss could be one reason for reduced hearing sensitivity and poor speech perception in the presence of noise. A third factor affecting the test results could be the gap in time between the onset of infection and audiological testing.

Upper respiratory infection, along with a cough and runny nose, is a common symptom seen in individuals infected with COVID-19. Because of oral cavity infection, there is a high chance of middle ear infection too, as the virus can travel from the oral cavity to the middle ear through the Eustachian tube. With treatment, however, the infection subsides and it can recover completely within a few months. That means that the hearing loss shown on audiometry soon after getting a COVID-19 infection might be a temporary effect and probably disappear after treatment. Many of the previously published studies were done during the active stage of infection, which might be the reason for the observed significant hearing loss [30]. In the present study, the assessment of the individuals was done within 1 to 6 months after infection, so the conductive component of the hearing loss is likely to have recovered completely over that time.

The severity of the infection and the length of stay at hospital might also be factors affecting the audiological findings [18,20]. All the participants in the present study had only a mild form of COVID-19 and none of them required hospitalisation. This might be another reason we found hearing sensitivity to be within the normal range.

TEOAE responses (with and without contralateral noise) showed no significant difference between individuals with or without COVID-19. This suggests that outer hair cell functioning is similar across both groups. TEOAE suppression in individuals with COVID-19 was similar to that in individuals without COVID-19, suggesting that the efferent auditory pathway was functioning similarly in both groups.

For context, it is worth mentioning studies on normal subjects, not on COVID patients. Here, there are several studies reporting on the application, reliability, and other factors affecting TEOAEs. One of them reported showed great stability of TEOAE thresholds in individuals up to 70 years old, with low variability within subjects – about 4 dB [31]. The contralateral inhibition of TEOAEs in young adults with normal hearing showed no significant effect of ear and gender on absolute TEOAE inhibition [32]. Lisowska and colleagues reported a decrease in the strength of the medial olivocochlear (MOC) system with increasing age in normal-hearing individuals; they also reported a decrease in OAE suppression in older individuals compared to young adults [33]. In a similar approach, Jedrzejczak and colleagues reported the reliability of contralateral suppression of TEOAEs using a commercial device in ears with and without spontaneous OAEs; they concluded that the presence of spontaneous OAEs does not seem to have an effect on TEOAEs, at least when measuring global or half-octave band responses [34].

Click-evoked ABRs in both ipsilateral and contralateral modes showed similar latency and amplitude in both groups, suggesting the normal functioning of afferent and efferent auditory pathways. Other studies in normal infants and children (non-COVID patients) have shown developmental changes of ipsilateral and contralateral ABRs [35]. Hatanaka and colleagues underlined the importance of contralateral recording of ABRs to identify developmental changes in infant auditory pathways. Another study by Kato and colleagues reported ABRs in normal healthy adults using monaural stimulation and ipsilateral and contralateral recordings [36]. Results of ipsilateral recording showed a small reduction for waves II and V, and a small increase for waves III and IV.

Speech perception in quiet and in noise showed similar performance between individuals with and without COVID-19 infection. The pattern of speech perception scores across SNRs was the same for both groups, suggesting that speech perception is not affected by the COVID-19 infection. The audiological test reports indicate there was no significant effect of mild COVID-19 infection on auditory system functioning. Studies on COVID patients report no deleterious effects on speech perception in noise.

However, there are several studies in the literature on the non-COVID population [37].

Another study examined speech perception in noise between sentences and prosody recognition [38]. Results showed that, as the SNR deteriorated, significant deterioration in the recognition of sentences as well as the word in sentences, whereas there were no deleterious effects on the prosody recognition with change in SNR [38]. Smith and colleagues examined why some listeners struggle to perceive speech-in-noise (SIN) despite having normal hearing sensitivity [39].

Limitations

A small sample size (30 participants in each group) was used for this study. The results should therefore be generalised with caution. This study compared two groups of participants, one group of participants with a history of COVID-19 infection and another group without COVID-19 infection. Comparing the same individuals before and after COVID-19 infection would have given better information about the effect of infection on the hearing system.

Conclusions

For individuals who have suffered mild COVID-19, testing showed values within the normal range for hearing thresholds (at conventional and extended high frequencies), TEOAE responses with and without contralateral noise, ABRs in ipsilateral and contralateral mode, and speech scores in quiet and at different SNRs. This suggests that, following mild COVID-19 infection, individuals are not likely to show a significant hearing-related issue after they have recovered.

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