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Assessment of cortical evoked potential (P300) and auditory brainstem response (ABR) in post-COVID-19 patients

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Abstract

Background The COVID-19 pandemic has had a substantial impact on many aspects of human health. There has been a major influence on cognitive capacities, including memory, attention, and cognitive skills for planning, organizing, and solving problems. Furthermore, it appears that the effects of COVID-19 may also impact the auditory system.

Objective To determine the effect of SARS-CoV-2 virus on both hearing and cognitive.

Patients and methods Eighty participants, ranging in age from 20 to 59, will be evaluated for their auditory and cognitive abilities using the following methods: ABR using a click stimulus presented at 90 dBnHL at a rate of 21.1 c/s, followed by a rate of 71.1 c/s; cortical auditory evoked potential (P300) using a tone burst stimulus (50 ms) that will produce an oddball paradigm; measurements of the waveforms' amplitude and latency will be made.

Results ABR recording for both ears showed significant difference between cases and controls as regarding absolute latencies of wave I, III, V, wave V (high rate), amplitude (low and high rates), amplitude ratio, and interaural latency differences (III, I-III, I-V), while P300 outcomes showed a statistically significant difference between cases and controls regarding P300 latency ($p < 0.05$), while for amplitude, a highly significant difference was found.

Conclusion COVID-19 can harm both the inner ear and the auditory pathway, and it has long-lasting effects on the auditory system and on cognitive processing and attention.

Keywords Cortical auditory evoked potential (P300), Auditory brainstem response (ABR), COVID-19, Cognitive processing

Background

In December 2019, an outbreak of the coronavirus disease, also known as COVID-19, occurred in Wuhan, China, and has since spread to other countries. On March 11, 2020, the World Health Organization (WHO) announced that the COVID-19 outbreak has developed into a pandemic. Chinese researchers discovered and sequenced the virus that caused COVID-19, also known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). They discovered that it was a novel coronavirus with a zoonotic origin since it shared a high degree of sequence identity with SARS-like coronaviruses produced from bats and pangolins [1].

Numerous facets of human health have been significantly impacted by the COVID-19 pandemic. Cognitive capabilities, such as memory, attention, and cognitive skills for organizing, planning, and problem-solving, have been significantly impacted [2].

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Moreover, it seems that COVID-19's effects can also affect the auditory system. Numerous investigations have documented cases of hearing impairment in virus-infected persons. To completely understand the relationship between this respiratory condition and its impact on hearing function, more research is still necessary [3].

Many hypotheses have been proposed to try and explain some of the uncertain probable causes for hearing complaints in COVID-19 individuals, including brainstem damage, inflammatory mechanisms, and hematopoietic tracts [4].

Since its initial description by Sutton et al., the P300, a component of event-related potential (ERP), has been the subject of substantial investigation [5]. An unusual paradigm stimulus that is connected to the brain's active mental processes, such as attention, perception, memory, and cognition, was used to elicit it [6]. An accurate evaluation of central auditory function, including the brain's cognitive process, is provided by this electrophysiologic test [7].

A non-invasive test called the auditory brainstem response (ABR) or brainstem auditory evoked potential (BAEP) is used to assess the auditory nerve route that runs from the inner ear to the brainstem [8].

Although COVID-19 is mostly a respiratory virus, it can also damage other organs, especially the auditory system. There have been multiple case reports of abrupt hearing loss, vertigo, and tinnitus during or after COVID-19.

Methods

This is a case-controlled study at the Audio-Vestibular Unit of our hospital. The study was ethically approved by the research ethics committee of the university.

Eighty people took part, split into two groups:

Forty post-recovery patients who tested positive for SARS-CoV-2 made up the study group. They were between the ages of 20 and 59, with a mean age of 36.75 (± 11.52) years. The 40 healthy adults in the control group ranged in age from 20 to 59 years, with a mean age of 38.53 (± 12.30) years.

Inclusion criteria:

- Post-COVID-19 patients who was confirmed positive for SARS-CoV-2 by nasopharyngeal RT-PCR swab
- Alert, cooperative, and average intelligence individuals

Exclusion criteria:

- Individuals with pre-existing hearing impairments or neurological disorders
- History of noise exposure or ototoxic medications
- Diabetic and hypertensive patients

Instrumentation

1. Itera II, Madsen Otometrics (GN Otometrics, Denmark) calibrated according to International Standard Organization (ISO) standards. TDH-39 head phones and radio-ear B-71 bone vibrator were used.
2. Neuro-Audio v.2010 (Neurosoft Ltd, Russia).

Each participant included in this study will be subjected to full history taking, otoscopic examination of both ears, pure-tone behavioral thresholds obtained by conventional pure-tone audiometry, air conduction thresholds obtained from 250 to 8000 Hz, and bone conduction thresholds obtained from 500 to 4000 Hz and speech reception threshold (SRT), using Arabic spondaic words. Word discrimination score (WDS), using Arabic phonetically balanced words [9]. The participants underwent also an electrophysiological evaluation consisting of auditory brainstem response (ABR) and cortical auditory evoked potential (P300) using the Neurosoft evoked potential system. The electrode montages were identical for both the ABR and P300 using three surface electrodes. The first was placed on the forehead (positive or active electrode), the second on the ipsilateral mastoid (negative or reference electrode), and the ground electrode was on the contralateral mastoid. The electrode impedance was kept below 5 K Ohms.

a)a)a)a)a)a)a)a)a)a) Auditory brainstem response

We used click stimulus with 100 μs duration presented independently to each ear through insert earphones with foam ear tips at a level of 90 dBnHL at a rate of 21.1 pulse/s (low rate) for waves I, III, and V, followed by a rate of 71.1 pulse/s (high rate) for wave V only.

The activity received from the electrodes was recorded by a differential amplifier and a second-stage amplifier; filters on both amplifiers were set at 100 and 3000 Hz. A total of 1024 sweeps was averaged separately under right and left ear stimulation. Time window: 10 ms.

b)b)b)b)b)b)b)b)b)b) Auditory P300 potential

Using the same electrode montage as used in ABR above, subjects were asked to identify the rare stimulus by pressing on button.

We used tone burst stimuli presented to the right ear via an insert phone, 50-ms tones presented at a rate of 1.1/s. For each condition, the standard stimulus was

presented with 80% probability and the target stimulus (rare stimulus) was presented randomly with 20% probability.

One hundred stimuli were delivered, with a 1–30 Hz filter. Time window: 500 ms.

Statistical methods

The statistical software for the social sciences (SPSS) version 28 (IBM Corp., Armonk, NY, USA) was used to code and enter the data. For quantitative data, the mean, standard deviation, median, minimum, and maximum were used to summarize the data; for categorical data, the frequency (count) and relative frequency (%) were used. The non-parametric Mann–Whitney and Kruskal–Wallis tests were used to compare quantitative variables. We used the chi-square (2) test to compare categorical data. When the anticipated frequency is less than 5, an exact test was utilized instead. The Spearman correlation coefficient was used to perform correlations between quantitative variables. The threshold of 0.05 for a p value was deemed statistically significant.

Results

Demographic data

The current study included 80 participants, arranged into two groups:

- Case group consisted of 40 participants who had recovered from COVID-19 and control group consisted of 40 healthy volunteers with no statistically significant difference was found in the age distribution between cases and controls ($p < 0.05$) (Table 1).

Regarding the symptoms of COVID-19 among the study group, the most prevalent symptom was tinnitus, hearing loss then vertigo.

Mild to moderate symptoms were observed in half of the cases (50.00%), while severe symptoms were reported in 45.00% of participants. Critical symptoms were observed in a smaller subset, constituting 5.00% of the cases (Fig. 1).

PTA showed a significant difference in all hearing thresholds between cases and controls at all frequencies. There are highly significant differences at frequencies (8 kHz in RT ear, 0.25 kHz, 4 kHz, 8 kHz in LT ear) (Tables 2 and 3).

For both ears, a significant difference was found in the SRT and discrimination between cases and controls, indicating that cases had a higher SRT and lower discrimination percentage compared to controls (Table 4).

Regarding auditory brainstem response (ABR) findings

ABR recording for both ears showed p values less than 0.05 regarding absolute latencies of wave I, III,

Table 1 The distribution of age among cases and controls

	Case					Control					*p* value
	Mean	SD	Median	Minimum	Maximum	Mean	SD	Median	Minimum	Maximum	
Age (years)	36.75	11.52	34.50	20.00	59.00	38.53	12.30	39.00	20.00	59.00	0.541

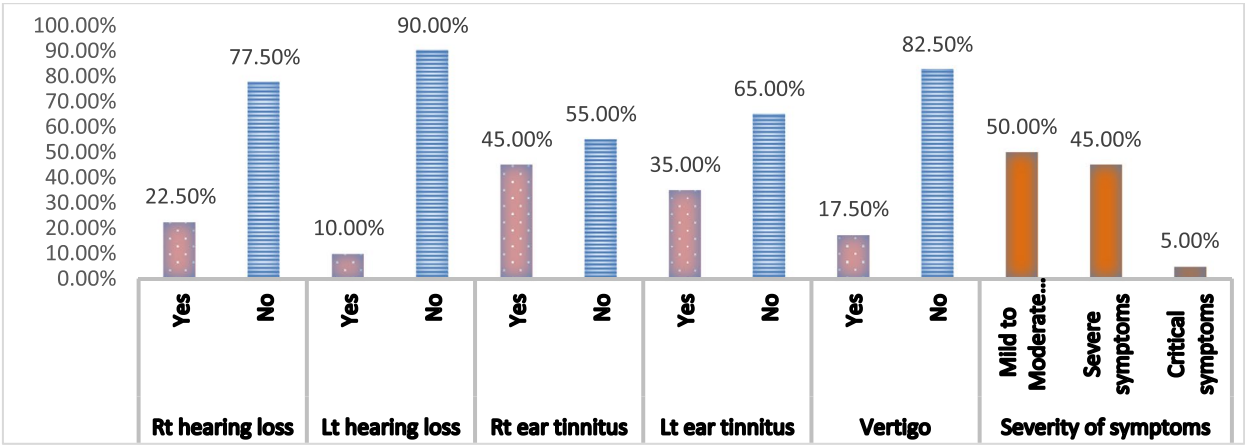

Fig. 1 The prevalence of hearing loss, tinnitus, vertigo, and severity of symptoms

Table 2 Comparison of PTA hearing thresholds (dBHL) between cases and controls at various frequencies for the RT ear

	Case					Control					*p* value
	Mean	SD	Median	Minimum	Maximum	Mean	SD	Median	Minimum	Maximum	
RT ear 0.25 kHz (dBHL)	16.13	9.09	15.00	5.00	35.00	9.75	2.52	10.00	5.00	15.00	0.001*
RT ear 0.5 kHz (dBHL)	16.75	8.51	15.00	5.00	30.00	11.38	3.75	10.00	5.00	20.00	0.006*
RT ear 1 kHz (dBHL)	18.00	8.97	15.00	5.00	35.00	12.00	4.05	10.00	5.00	20.00	0.003*
RT ear 2 kHz (dBHL)	18.00	8.61	15.00	5.00	35.00	12.63	3.92	12.50	5.00	20.00	0.008*
RT ear 4 kHz (dBHL)	21.62	13.08	20.00	5.00	65.00	12.87	4.22	12.50	5.00	20.00	0.003*
RT ear 8 kHz (dBHL)	22.38	12.19	15.00	5.00	45.00	12.25	4.52	10.00	5.00	25.00	< 0.001*
Average (RT ear) (dBHL)	18.59	9.23	16.88	6.25	36.25	12.22	3.65	11.88	6.25	20.00	0.004*

* *p* significant < 0.05

Table 3 Comparison of PTA hearing thresholds (dBHL) between cases and controls at various frequencies for the LT ear

	Case					Control					*p* value
	Mean	SD	Median	Minimum	Maximum	Mean	SD	Median	Minimum	Maximum	
LT ear 0.25 kHz (dBHL)	15.50	7.58	15.00	5.00	30.00	10.00	2.53	10.00	5.00	15.00	< 0.001*
LT ear 0.5 kHz (dBHL)	16.38	8.62	15.00	5.00	35.00	11.63	3.82	10.00	5.00	20.00	0.015*
LT ear 1 kHz (dBHL)	17.63	8.99	15.00	5.00	35.00	12.13	4.22	10.00	5.00	20.00	0.006*
LT ear 2 kHz (dBHL)	18.62	8.99	15.00	5.00	35.00	12.75	3.75	12.50	5.00	20.00	0.002*
LT ear 4 kHz (dBHL)	20.75	10.16	15.00	10.00	45.00	12.75	4.23	10.00	5.00	20.00	< 0.001*
LT ear 8 kHz (dBHL)	19.87	9.77	20.00	5.00	40.00	12.00	4.21	10.00	5.00	25.00	< 0.001*
Average (LT ear) (dBHL)	18.34	8.72	15.00	7.50	36.25	12.31	3.61	11.88	7.50	20.00	0.002*

* *p* significant < 0.05

Table 4 Comparison of speech recognition threshold (SRT) and discrimination (%) in cases and controls

	Case					Control					*p* value
	Mean	SD	Median	Minimum	Maximum	Mean	SD	Median	Minimum	Maximum	
SRT (dBHL) RT ear	17.75	8.00	15.00	10.00	35.00	13.00	3.54	10.00	10.00	20.00	0.012*
SRT (dBHL) LT ear	17.50	7.84	15.00	10.00	35.00	13.12	3.52	12.50	10.00	20.00	0.022*
Discrimination (%) RT ear	94.60	2.80	96.00	88.00	96.00	96.00	0.00	96.00	96.00	96.00	0.002*
Discrimination (%) LT ear	94.30	3.38	96.00	84.00	96.00	96.00	0.00	96.00	96.00	96.00	0.001*

* reflect statistically significant

V, wave V (high rate), amplitude (low and high rates), amplitude ratio, and interaural latency differences (III, I-III, I-V), indicating that there is a significant difference between cases and controls for these variables (Tables 5, 6, and 7).

Regarding the ABR results for cases with mild to moderate symptoms, severe symptoms, and critical symptoms, a significant difference was found between the three groups at wave V latency and interpeak latencies (III-V and I-V) of the right ear (Table 8).

For cortical evoked potential (P300) findings

P300 outcomes showed a statistically significant difference between cases and controls regarding P300 latency ($p < 0.05$), while for amplitude, a highly significant difference was found ($p < 0.001$).

When comparing P300 latency among cases with mild to moderate symptoms versus those with severe symptoms, a significant difference was observed ($p < 0.05$). However, the changes in amplitude were not

Table 5 Comparison of auditory brainstem response (ABR) results of right ear for cases and controls

	Case					Control					*p* value
	Mean	SD	Median	Minimum	Maximum	Mean	SD	Median	Minimum	Maximum	
Wave I latency (RT ear)	1.46	0.18	1.47	1.16	1.80	1.31	0.16	1.31	1.02	1.56	< 0.001*
Wave III latency (RT ear)	3.48	0.13	3.45	3.23	3.71	3.36	0.15	3.39	3.07	3.81	0.001*
Wave V latency (RT ear)	5.31	0.25	5.28	4.91	5.74	5.15	0.14	5.11	5.00	5.61	0.004*
IPL I-III (RT ear)	2.02	0.16	2.01	1.82	2.54	2.06	0.17	2.00	1.88	2.59	0.170
IPL III-V (RT ear)	1.83	0.20	1.83	1.45	2.49	1.79	0.15	1.81	1.54	2.35	0.312
IPL I-V (RT ear)	3.85	0.26	3.88	3.41	4.53	3.84	0.21	3.83	3.52	4.47	0.773
Wave V (high rate) (RT ear)	5.57	0.31	5.57	5.08	6.19	5.38	0.16	5.37	5.05	5.98	0.001*
Amplitude (μv) V-Va (low rate) (RT ear)	0.60	0.24	0.59	0.05	0.98	0.48	0.20	0.47	0.13	0.91	0.018*
Amplitude (μv) V-Va (high rate) (RT ear)	0.66	0.31	0.72	0.13	1.08	0.42	0.20	0.39	0.12	0.87	0.001*
Amplitude ratio RT ear	3.68	0.46	3.47	3.10	4.84	4.00	0.51	3.82	3.26	4.92	0.001*

* reflect statistically significant

Table 6 Comparison of auditory brainstem response (ABR) results of left ear for cases and controls

	Case					Control					*p* value
	Mean	SD	Median	Minimum	Maximum	Mean	SD	Median	Minimum	Maximum	
Wave I latency (LT ear)	1.40	0.14	1.37	1.19	1.72	1.22	0.15	1.17	1.02	1.56	< 0.001*
Wave III latency (LT ear)	3.56	0.18	3.54	3.18	3.89	3.40	0.12	3.42	3.07	3.76	< 0.001*
Wave V latency (LT ear)	5.30	0.22	5.27	5.00	5.70	5.10	0.11	5.06	5.00	5.61	< 0.001*
IPL I-III (LT ear)	2.16	0.21	2.17	1.72	2.51	2.18	0.17	2.27	1.88	2.46	0.373
IPL III-V (LT ear)	1.73	0.16	1.72	1.41	2.11	1.70	0.12	1.65	1.56	2.06	0.320
IPL I-V (LT ear)	3.89	0.26	3.90	3.49	4.34	3.88	0.14	3.91	3.59	4.31	0.985
Wave V (high rate) (LT ear)	5.69	0.29	5.61	5.24	6.22	5.39	0.13	5.41	5.04	5.82	< 0.001*
Amplitude (μv) V-Va (low rate) (LT ear)	0.55	0.22	0.51	0.18	0.92	0.43	0.21	0.44	0.12	0.85	0.036*
Amplitude (μv) V-Va (high rate) (LT ear)	0.56	0.21	0.50	0.23	1.06	0.36	0.16	0.37	0.13	0.77	< 0.001*
Amplitude ratio LT ear	3.81	0.39	3.85	3.03	4.29	4.23	0.43	4.34	3.33	4.93	< 0.001*

* reflect statistically significant

Table 7 Comparison of interaural latency differences between cases and controls

	Case					Control					*p* value
	Mean	SD	Median	Minimum	Maximum	Mean	SD	Median	Minimum	Maximum	
Interaural latency difference I	0.16	0.14	0.10	0.01	0.48	0.11	0.10	0.08	0.00	0.24	0.160
Interaural latency difference III	0.12	0.09	0.00	0	0.39	0.08	0.07	0.06	0.00	0.32	0.001*
Interaural latency difference V	0.13	0.11	0.04	0	0.58	0.08	0.11	0.02	0	0.61	0.455
Interaural latency difference I-III	0.22	0.20	0.16	0	0.67	0.18	0.15	0.10	0.01	0.56	0.020*
Interaural latency difference III-V	0.16	0.15	0.12	0	0.58	0.14	0.07	0.16	0	0.29	0.825
Interaural latency difference I-V	0.21	0.17	0.18	0	0.64	0.15	0.14	0.11	0.01	0.85	0.039*
Interaural latency difference wave V (high rate)	0.14	0.14	0.01	0	0.54	0.11	0.13	0.08	0.00	0.69	0.613

* reflect statistically significant

statistically significant between these groups ($p > 0.05$) (Tables 9 and 10).

There was a strong positive correlation between the duration of recovery and P3 latency ($r = 0.705$, $p < 0.001$), indicating that as the duration of recovery increases, the P3 latency also tends to increase (Fig. 2).

Discussion

Numerous body systems are significantly impacted by the COVID-19 virus. Research has indicated that COVID-19 not only causes respiratory symptoms but also affects the neurological and auditory systems [10]. Lately, there has been increased interest in the evaluation of auditory brainstem response (ABR) and cortical evoked potential (P300) in patients recovering from COVID-19 [11].

Therefore, in order to better understand potential neurological and auditory repercussions, this study intends to evaluate P300 and ABR in persons who have recovered from COVID-19. According to this study, the cases' audiological symptoms included vertigo, hearing loss, and tinnitus, as illustrated in Fig. 1.

After comparing our results to previous research, AlJasser et al. [12], found that 8% of COVID-19 cases had hearing or tinnitus deterioration, while 2% of cases had tinnitus resolve after the acute period. However, rotatory vertigo was reported in 5% of COVID-19 patients, a notably higher frequency than in the control group (1.1%).

Tinnitus was the most frequently reported symptom (39%), followed by hearing loss (11%), and dizziness (10%) was the least prevalent symptom, according to Dharmarajan et al. [13].

Patients with COVID-19 may experience hearing loss, tinnitus, or vertigo for a variety of complicated and poorly understood reasons. According to Jafari et al. [14], there could be a number of factors, such as viral invasion, inflammation, vascular difficulties, neurological involvement, immunological reactions, drug side effects, systemic impacts, pre-existing disorders, and individual variability.

Our results are in opposition to those of Gallus et al. [15], who found no variations in PTA between the patient and control groups ($p = 0.094$). But among COVID-19 patients, the only frequency with significantly greater thresholds was 0.25 kHz ($p < 0.016$), whereas the thresholds for 2 kHz (p 0.042) and 4 kHz (p 0.029) were significantly higher in the control group.

The discrepancy between our research and the conclusions of Gallus et al. [15], may have resulted from the COVID-19 patients' assessments being completed at various times, which could have affected the outcomes. Depending on the infection or recovery stage, COVID-19 individuals may experience varied manifestations of hearing impairment.

The speech recognition threshold (SRT) and discrimination percentages between post-COVID-19 cases and controls showed significant differences in our study (Table 4), indicating that speech recognition and discrimination may be difficult for people recovering from COVID-19. Numerous factors, such as the direct effect of the virus on the auditory system, immune-mediated inflammation, possible ototoxic effects of COVID-19 medications, individual differences in the response to the virus, psychosocial factors, and the long-term persistence of symptoms, may be responsible for these challenges [10].

A related study by Boboshko et al. [16] highlighted the possible long-term impact on speech perception in post-COVID-19 persons by finding a noteworthy number of patients reporting problems in recognizing monosyllabic syllables, both in quiet and noisy surroundings.

This study reveals significant differences in the auditory brainstem response (ABR) absolute latencies (I, III, V) between the two groups, as well as the effects of high-rate stimulation on wave V, amplitude, and amplitude ratio in both ears. These results imply that the

Table 8 Comparison of ABR results between COVID-19 cases with mild to moderate symptoms, severe symptoms, and critical symptoms of the right ear

	Severity of symptoms															*p* value
	Mild to moderate symptoms					Severe symptoms					Critical symptoms					
	Mean	SD	Median	Minimum	Maximum	Mean	SD	Median	Minimum	Maximum	Mean	SD	Median	Minimum	Maximum	
Wave I latency (RT ear)	1.45	0.22	1.43	1.16	1.80	1.45	0.15	1.47	1.24	1.80	1.60	0.01	1.60	1.59	1.60	0.328
Wave III latency (RT ear)	3.47	0.14	3.44	3.23	3.70	3.47	0.12	3.44	3.31	3.70	3.66	0.08	3.66	3.60	3.71	0.171
Wave V latency (RT ear)	5.40	0.27	5.30	5.00	5.74	5.19	0.19	5.19	4.91	5.58	5.40	0.04	5.40	5.37	5.42	0.035*
IPL I-III (RT ear)	2.01	0.18	1.99	1.82	2.54	2.02	0.14	2.03	1.83	2.20	2.06	0.07	2.06	2.01	2.11	0.755
IPL III-V (RT ear)	1.93	0.22	1.90	1.53	2.49	1.72	0.12	1.71	1.45	1.88	1.74	0.04	1.74	1.71	1.77	0.004*
IPL I-V (RT ear)	3.95	0.28	3.94	3.44	4.53	3.74	0.21	3.79	3.41	4.05	3.80	0.03	3.80	3.78	3.82	0.042*
Wave V (high rate) (RT ear)	5.64	0.32	5.59	5.11	6.19	5.47	0.27	5.56	5.08	5.93	5.75	0.14	5.75	5.65	5.85	0.190
Amplitude (μv) V-Va (low rate) (RT ear)	0.52	0.22	0.59	0.05	0.76	0.68	0.24	0.74	0.25	0.98	0.63	0.25	0.63	0.45	0.80	0.123
Amplitude (μv) V-Va (high rate) (RT ear)	0.55	0.29	0.45	0.13	1.08	0.79	0.29	0.93	0.19	1.00	0.57	0.39	0.57	0.30	0.85	0.080
Amplitude ratio RT ear	3.78	0.54	3.73	3.19	4.84	3.61	0.36	3.49	3.10	4.27	3.38	0.01	3.38	3.38	3.39	0.730

* reflect statistically significant

Table 9 Comparison of cortical evoked potentials (P300) latencies (ms) and amplitudes (μv) between cases and controls

	Case					Control					*p* value
	Mean	SD	Median	Minimum	Maximum	Mean	SD	Median	Minimum	Maximum	
Latency (ms)	295.80	29.19	293.70	250.00	341.30	276.92	21.15	272.40	252.20	310.50	0.004*
Amplitude (μv)	5.39	2.28	4.60	1.70	12.50	19.83	5.75	19.95	10.30	29.50	< 0.001*

* reflect statistically significant

cases had lower amplitude ratios, higher wave V amplitudes in both low and high rates, and delayed wave I, III, and V (low rate and high rate) latency in comparison to the controls (Tables 5 and 6).

Rather than being the result of brainstem or neurological pathology, the prolongations in I, III, and V absolute latencies in the test group are thought to be the result of cochlear damage at high frequencies.

Additionally, interaural latency differences (III, I-III, and I-V) between the two groups differed significantly (Table 7). These results suggest possible differences in the conduction of the auditory pathway and neural response, which could influence the timing of auditory processing and signify aberrant auditory processing.

In line with our research, Öztürk et al. [17], discovered a noteworthy distinction ($p < 0.05$) in the absolute latencies of I, III, and V among the groups. In contrast to our findings, no statistically significant difference was observed in the I-III, III-V, and I-V interpeak latencies between the groups ($p > 0.05$).

Only the interpeak latencies of waves III–V showed a significant difference between the groups, according to Gedik et al. [18], Variations in auditory pathway conduction measurement may result in differences in interpeak latencies, wave V high rate, amplitude, and amplitude ratio, and other factors may impact interpretation in one study relative to another. These variables include variations in the age, gender, and clinical characteristics of the individuals as well as variations in the electrode placements, stimulation parameters, and statistical techniques applied. Contrasting results could also be caused by slight variations in signal processing techniques or peak detection criteria. Furthermore, differences in statistical power and sample size may have an impact on the capacity to identify meaningful differences. Random variation may still have an impact on the study's conclusions in spite of these precautions.

In contrast, the ABR latency and amplitude results between the groups of people with and without COVID-19 did not reveal a statistically significant difference, according to Apeksha et al. [19]. This study only looked at minor COVID-19 disorders, which could be the reason for the contrast that was discovered.

According to Table 8's data, there is a statistically significant difference between COVID-19 cases with mild to moderate symptoms, severe symptoms, and critical symptoms in terms of wave V latency and interpeak latencies I-V and III-V in the right ear. These results imply that the degree of COVID-19 symptoms may affect how auditory signals are processed by the brain and result in changes to how those signals are sent and processed at the brainstem level.

On the other hand, Hassani et al. [20] show that, in mild to moderate coronavirus disease cases, there were no significant differences in ABR wave latencies, interpeak intervals, or amplitudes at either the standard or high rate of stimulus presentation. However, in severe cases, they report sudden SNHL.

Our results reveal statistically significant variations in the amplitude and latency of the cortical evoked potential (P300) between the post-COVID-19 subjects and the control group. Particularly, cases had a greater mean delay value, indicating that the two groups' cognitive processes differed. Slower cognitive processing speed, which is essential for tasks involving attention and memory, may be implied by this delayed P300 latency. Furthermore, a statistically significant variation in P300 amplitude was noted, suggesting that the mean amplitude of patients was considerably lower in comparison to controls. This reduced cognitive response raises the possibility of variations in attention- and cognitive-processing-related brain activity between the two groups (Table 9).

Comparing patients with proven SARS-CoV-2 infection and moderate hyposmia symptoms to healthy controls, Clemente et al. [21], which used visual P3 as an event-related potential paradigm, revealed similar delays in response latency to deviant stimuli. Responses to deviant stimuli differed significantly from those to target stimuli, despite the similarities in responses. This delayed reaction to abnormal stimuli could be a sign of altered cognitive processing in COVID-19-affected individuals.

There could be other reasons for the observed variations in P300 responses between COVID-19 patients. The list of these includes direct viral effects, inflammatory reactions, microvascular abnormalities, and neurotransmitter dysregulation. According to Nalbandian

Table 10 Comparison of p300 latency (ms) and amplitude p3-p3a (μv) differences between cases with mild to moderate symptoms and cases with severe symptoms

	Mild to moderate symptoms					Severe symptoms					*p* value
	Mean	SD	Median	Minimum	Maximum	Mean	SD	Median	Minimum	Maximum	
p3 latency (ms)	274.72	18.63	279.15	250.00	314.90	323.90	10.83	322.80	309.60	341.30	< 0.001*
Amplitude p3-p3a (μv)	5.20	2.59	4.20	1.70	12.50	5.65	1.86	4.90	3.90	11.00	0.217

* reflect statistically significant

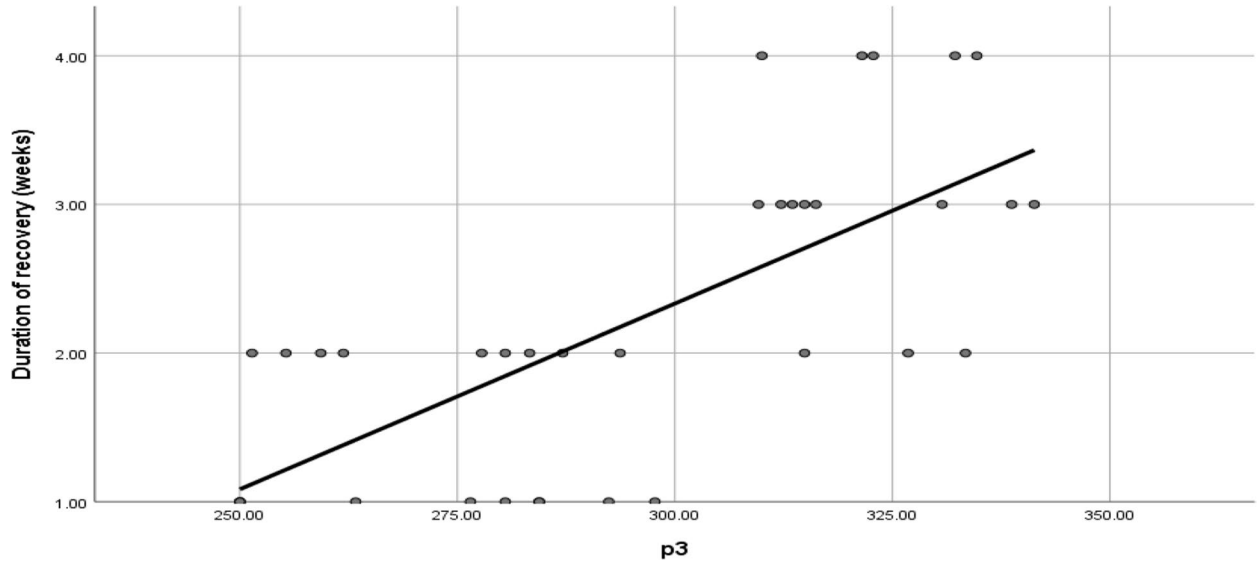

Fig. 2 Regression line shows a positive correlation between the duration of recovery from COVID-19 and P3 latency

et al. [22], COVID-19 may affect serotonin and dopamine systems, which may impact neural activity and contribute to changes in evoked potentials. Additionally, COVID-19 may disrupt neural networks that are involved in cognitive processes like attention and memory.

P300's low amplitude and delayed latency could be signs of problems in these networks. Delay in latency and reduction in amplitude in P300 responses could be caused by direct viral effects on brain structures, particularly those related to cognitive processing. Whether systemic or localized, inflammation can change cognitive processing and interfere with neuronal signaling [23].

However, Da Silva Soares et al. [24], used speech stimuli to measure cognitive potential and did not uncover any appreciable variations in P300 values across the groups. This discrepancy can result from the use of speech stimuli, which is explained by variations in the features of the stimuli and study design. The differences in P300 parameter results could be caused by differences in the type of stimuli, sensory modality (voice vs. audio), cognitive demands, task specificity, participant characteristics, experimental methodology, sensitivity of measurement techniques, sample size, and temporal features.

The results of our investigation also shed light on how P300 values are affected by the severity of COVID-19. More specifically, compared to those with mild to moderate symptoms, those with severe symptoms showed noticeably longer latencies for P3. While there was no statistically significant variation in P300 amplitude between the two groups, the findings imply that the severity of COVID-19 may have an effect on cognitive processing and attention, which could result in delayed cognitive responses. The observed variations in delay highlight how crucial it is to take COVID-19 severity into account when assessing cognitive and neurological function (Table 10).

Studies by Altuna et al. [25] and Shaddad et al. [26] have shown a high incidence of cognitive impairment in severe COVID-19 cases, which is similar to our finding. Additionally, cognitive symptoms have been shown to persist in people with mild or asymptomatic histories, which has a negative impact on functional abilities and work performance.

This resemblance may be the result of both parties' emphasis on people with more severe symptoms. In severe cases, there are immunological activation, persistent inflammation, and neurological involvement that impair cognition. Hypoxia-related damage and compromised cognitive function may arise from COVID-19's effects on respiratory distress, virus propagation, hypoxia, and organ malfunction [27].

However, Khieukhajee et al. [28] could not discover any appreciable variations in cognitive assessments between the patients and the healthy controls. This discrepancy could be caused by variations in the study population, the intensity of COVID-19 symptoms, the methods and procedures used for cognitive assessment, and the existence of confounding variables such mental health issues, drugs, or pre-existing cognitive impairments. These variables could affect the selection of cognitive tests, when they are administered, and how the findings are interpreted.

We also investigated the relationship between P3 latency and amplitude and the length of time it takes to recover from COVID-19. The period of recovery and P3 delay showed a high positive association ($r=0.705$) and a statistically significant difference, according to the data. P3 latency also tended to rise as recovery duration did (Fig. 2), indicating that longer recovery times might be linked to cognitive processing delays. Long-term impacts on the central nervous system, neuroinflammation, and neuronal injury are some of the factors that contribute to this [29].

The modest and non-statistically significant association between recovery duration and P3 amplitude suggests that recovery time may not have a substantial effect on the strength of the cognitive response. This can be the result of individual variations in the recovery of brain function or neural recovery [30].

Conclusion

1. COVID-19 can harm both the inner ear and the auditory pathway, and it has long-lasting effects on the auditory system, particularly at high frequencies.
2. Differences in ABR characteristics between the controls and the patients demonstrate how COVID-19 affects auditory processing.
3. Variations in P300 latency and amplitude between cases and controls demonstrate the impact of COVID-19 on cognitive processing and attention.

Recommendations

To ensure generalizability, more research utilizing bigger sample sizes and diverse individuals is required to investigate the mechanisms behind COVID-19-related auditory symptoms and their effects on brain processing and cognitive abilities.

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Authors' contributions
MH and NH contributed with sharing in writing the paper and submission and correspondence. RF and ZE contributed with application of the idea, steps of the methods, and supervising the study work. NH and MH supervised the work. RF and ZE contributed with data collection and writing the paper. All authors have read and approved the manuscript.

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Availability of data and materials
The datasets during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate.
This study has been approved by the Research Ethics Committee of Kasr Al-Aini Hospital, Cairo University (number MS-358–2022). An informed written consent to participate in the study was provided by all participants.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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