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# Central auditory functions in post-COVID-19 adults; a case control study

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## Abstract

**Background** This study aimed to evaluate the central auditory abilities in post-coronavirus disease 2019 (COVID-19) adults by using Central Auditory Tests (CATs). This study included a complaining group (GI), a non-complaining group (GII), and a control healthy group (GIII). All subjects were evaluated using CATs

**Results** Results demonstrated statistically significant differences across groups as regards Speech Perception in Noise Test (SPIN), Duration Pattern Sequence Test (DPT), Gap in Noise Test (GIN), and Memory Test (ANOVA,  $p$ -value  $\leq 0.05$ ). The post-hoc test revealed that, except for recognition memory, both study groups showed statistically significant differences from the control group. Also, significant differences were detected between both GI and GII groups regarding SPIN<sup>-10</sup> signal-to-noise ratio (S/N), DPT, GIN threshold, memory for content, and memory for sequence

**Conclusions** COVID-19 led to central auditory processing disorders (c)APD.

**Keywords** Auditory processing disorders (APD), Central auditory tests (CATs), Coronavirus disease 2019 (COVID-19), Duration Pattern Sequence Test (DPT), Gap in Noise Test (GIN), Speech Perception in Noise (SPIN)

## Background

In December 2019, the coronavirus emerged and began its rapid spread across numerous countries [1]. Many studies have discussed otological, rhinological, and laryngeal issues related to COVID-19 disease [2–5]. However, little research highlighted the central auditory processing deficit post-Covid infection. The term "post-COVID conditions" included a wide range of physical and mental health consequences experienced by some patients when they presented four weeks or more after COVID-19 disease, according to the United States Centers for Disease Control and Prevention [6]. Fatigue and "brain fog" are among the most commonly reported post-COVID-19 symptoms [7]. The term "brain fog" was used to describe difficulty concentrating, memory problems, and

sometimes confusion during the COVID-19 pandemic [8]. The profile of post-COVID-19 cognitive impairment involves attention and planning difficulties, decreased information processing speed, and deficits in short-term memory, abstraction, orientation [9], and sustained attention [10]. COVID-19 disease presents some peculiar characteristics. The presence of cognitive symptoms does not have a clear temporal relation with other symptoms or their severity. In patients with COVID-19 infection, cognitive symptoms may persist longer than other symptoms [11].

Accordingly, this work was designed to evaluate the central auditory abilities in post-COVID-19 adults using different Central Auditory Tests (CATs).

## Methods

This is a prospective case–control study. Post-COVID-19 complaining adults were obtained from our university hospital's outpatient Audio-Vestibular Unit (ORL department). Post-COVID-19 non-complaining subjects were relatives of post-COVID-19 complaining patients.

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Normal subjects were volunteers or relatives of patients and hospital medical staff.

Fifty subjects were included in this study, with the age range of 18–45 years. Subjects were divided into three groups: The first was the complaining group (consisting of 20 post-COVID-19 complaining adults (GI)), and the second was the non-complaining group (consisting of 10 post-COVID-19 non-complaining adults (GII)). They all had at least one COVID-19 attack during the last 4 months., diagnosed by PCR. All subjects came for testing after recovery. The inclusion criteria of the study groups (GI and GII) included: (1) Age ranged from 18 to 45 years with normal peripheral hearing. (2) Normal middle ear function. The Exclusion criteria included: (1) Patients who had a history of hearing loss or history of any known cause of hearing loss or central auditory processing disorders (CAPD). (2) History of cognitive complaints regarding memory and attention prior to COVID-19 infection. (3) Patients with a history of past neurological and psychological illness. (4) Refusal to participate in the study.

The third group was the Control group (GIII). It consisted of 20 healthy adults. They all had no complaints regarding hearing or vestibular systems. The inclusion criteria included (1) normal peripheral hearing. (2) Normal middle ear function. (3) seronegative test for antibody for COVID-19. Their exclusion criteria included: (1) seropositive antibody test for COVID-19. (2) History of cognitive complaints regarding memory and attention. (3) History of any neurological, psychological, systemic, or endocrinal diseases, and (4) Refusal to participate in the study.

### Equipment

Sound-treated room: Transacoustic Model No RE241. Two-channel pure tone audiometer: Grasson-Stadler version 61 clinical audiometer. Immittance: Interacoustic AT235H and CD player (Thomason cs96) connected to the audiometer and adjusted to deliver central speech material.

### Materials

CDs of CATs including Speech Perception in Noise Test (SPIN), Duration Pattern Test (DPT), Gap in Noise Test (GIN), and Auditory Memory Test.

All subjects included in this study were submitted to:

- I. Full audiological evaluation including (1) Full audiological history and for patients in the study groups (groups I and II), a detailed history of COVID-19 infection was taken. (2) Otological examination and Basic audiological evaluation.
- II. Central Auditory Processing (CAP) Questionnaire for adults [12]: It consisted of questions about CAPD in adults. The answers to questions were either yes or no. This questionnaire was applied to detect post-COVID-19 patients complaining of CAPD.
- III. CATs: Speech Perception in Noise test (SPIN) at varying S/N ratios (+10, 0, and -10) [12], Duration Pattern Test [DPT] [13], Gap in Noise Test [GIN] [14], and Auditory Memory Tests [15] including Recognition Memory, Memory for Content Test and Memory for Sequence Test.

### Statistical analysis

Data collection and analysis were conducted using IBM® SPSS software, version 21. The analysis encompassed two primary statistical approaches: Descriptive statistics, which included the calculation of the number (No), percentage (%), mean ( $\bar{x}$ ), and standard deviation; and Analytical statistics, where various tests were applied. The Kolmogorov–Smirnov test determined data normality, while the Fisher exact test assessed gender differences between groups. The paired t-test compared matched pairs of normally distributed data. Group analysis involved one-way Analysis of Variances (one-way ANOVA) for normally distributed data, supplemented by Tukey's multiple comparison test as a post-hoc measure. Pearson correlation assessed the relationships between variables. Statistical significance was established at a two-sided *P*-value of less than 0.05.

## Results

### Age and gender distribution

All subjects in this work were matched as regards age. GI included 20 subjects, and their age ranged from 20 – 34 with a mean and SD of  $26.95 \pm 3.59$ . In contrast, the GII included 10 subjects with ages ranging from 21 – 34 with a mean of 27.40 and  $SD \pm 4.45$ . The control group (GIII) included 20 subjects; their age ranged from 21 to 31, with a mean  $\pm SD$  of  $25.80 \pm 2.19$  years. There was no statistically significant difference regarding age (*p*-value > 0.05) among all studied groups.

All groups were matched for gender distribution with no statistically significant difference (*p* > 0.05). In the study group (I), females (19/20 = 95%) were more than males (1/20 = 5%). Similarly, the study group (II) also showed a greater female presence (9/10 = 90%) versus males (1/10 = 10%). The control group III mirrored the gender distribution of group I, with females constituting 95% (19 out of 20) and males 5% (1 out of 20).

**Characters of COVID-19 attacks**

The duration of COVID-19 attacks ranged from 7 -25 days, with the mean ± SD of 13.56 ± 4.64 days. In contrast, the time between COVID-19 acute attack/s and time of examination ranged from 6 – 23 weeks with the mean ± SD of 13.80 ± 6.36 weeks. As regards the number of COVID-19 attacks, 19 subjects (63.3%) suffered from one attack of COVID-19, 10 subjects (33.3%) suffered from 2 attacks, and only one subject (3.3%) suffered from 3 attacks.

**Oxygen (O<sup>2</sup>) saturation during the last acute COVID-19 attack**

O<sup>2</sup> saturation during COVID-19 attack in patients of the study group (I) ranged from 92%—98% with a mean ± SD of 94.65 ± 1.53. While in the study group (II), it ranged from 94%—98% with a mean ± SD of 96.30 ± 1.56 with statistically significant differences between the 2 groups (GI and GII) (*p* = 0.01, *t* = -2.761) (Table 1).

**Results of the CAP Questionnaire for adults**

According to the Arabic CAP Questionnaire for adults, memory problems were the most common complain, followed by lack of attention and difficulty in understanding speech in noise (Shown in Fig. 1).

**Table 1** Oxygen saturation among complaining and non-complaining groups

Oxygen saturation	Post-covid complaining group	Post-covid noncomplaining group	t	P
Range	92—98	94—98	-2.761	0.010*
Mean ± SD	94.65 ± 1.53	96.30 ± 1.56		

t: independent sample t-test\*; P value is significant at the 0.05 level. P ≤ 0.05 is significant P ≤ 0.001 is highly significant

As there was no statistically significant difference between right and left ears in all groups regarding all tests (paired t-test *p*-value > 0.05), the data from both ears were combined and averaged for subsequent statistical analysis.

**Basic audiological evaluation in the two study groups and the control group**

All tested groups had normal Pure Tone thresholds at all tested frequencies shown in Fig. 2, normal speech reception thresholds, and normal word discrimination.

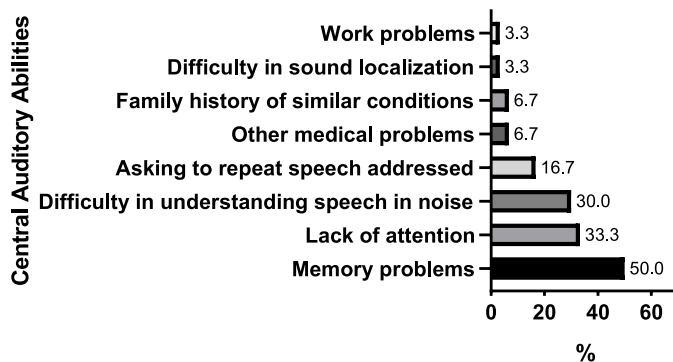
**Results of the (CATs) in all studied groups**

Results of the present study revealed a statistically significant decrease in the scores of CATs in both study groups compared to the control group. ANOVA test revealed statistically significant differences among the studied groups (*p* ≤ 0.05) regarding SPIN-SNR<sup>zero</sup>, SPIN-SNR<sup>-10</sup>, DPT, GIN score, GIN threshold, and memory test. The post-hoc test revealed that, with the exception of recognition memory (MR), both study groups showed statistically significant differences from the control group (lower scores in the study groups than in the control group). Also, statistically significant differences were detected between both GI (complaining) and GII (non-complaining) regarding SPIN-SNR<sup>-10</sup>, DPT, GIN threshold, memory for content (MC) and memory for sequence (MS).

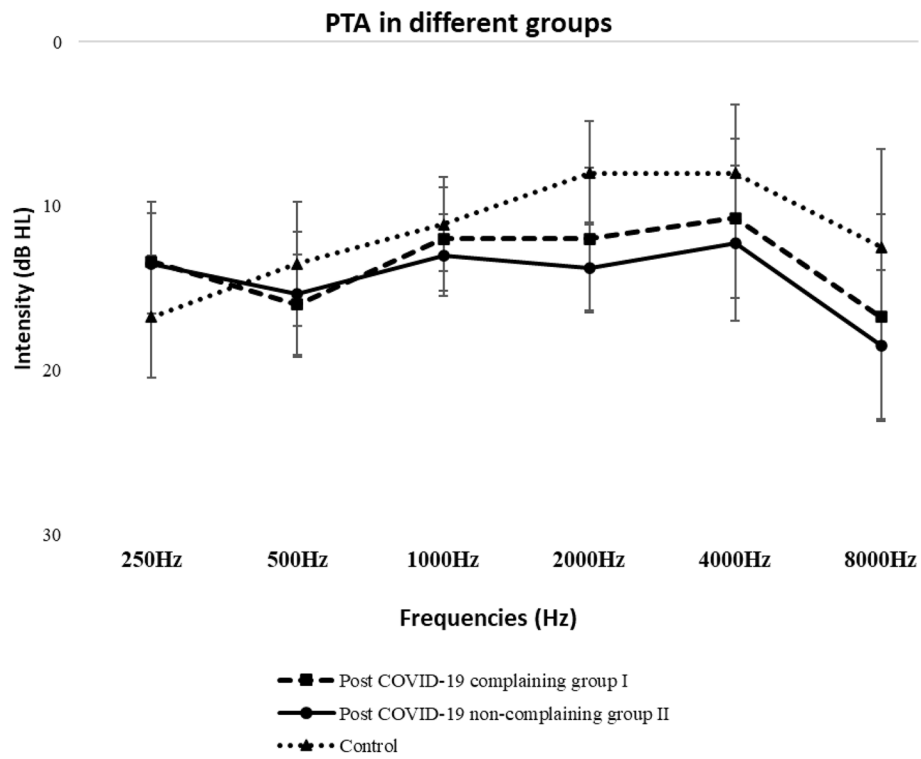
**Correlations**

There was a statistically significant positive correlation between [GIN score and time lag (in weeks) between acute attacks and date of examination] as shown in Fig. 3. Also, there was a statistically significant positive correlation between (SPIN-SNR<sup>-10</sup> and O2 saturation during the acute attack) as shown in Fig. 4.

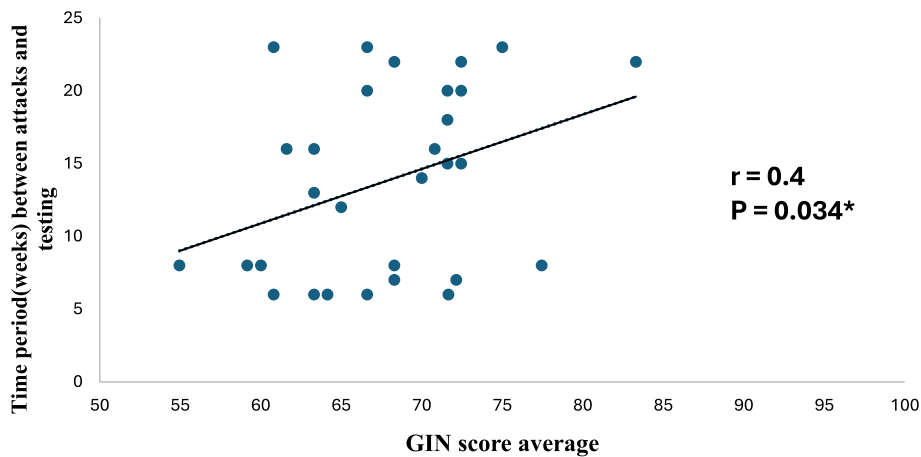
**Central Auditory Processing Questionnaire For Adults**



**Fig. 1** Central Auditory Processing Questionnaire for adults



**Fig. 2** Line graph showing the different means of the PTA at different tested frequencies. PTA: pure tone audiometry

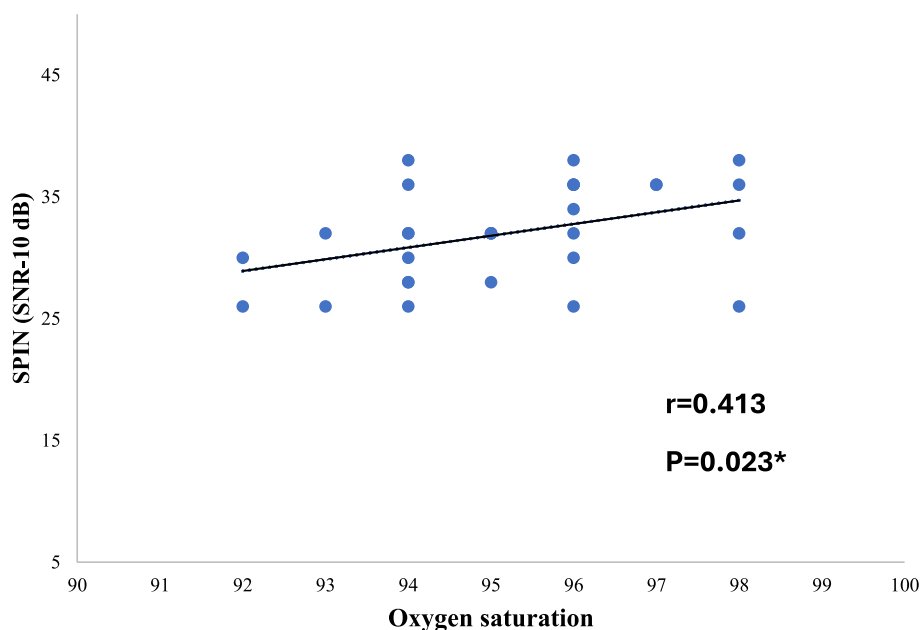


**Fig. 3** Correlation between GIN score and the time period (weeks) between date of acute attacks and date of examination (weeks) in the study groups (I & II) (N=30). GIN: Gap In noise

However, there were no statistically significant correlations between other parameters (CATs) and duration of attacks, number of attacks, duration between attacks and testing and O<sup>2</sup>-saturation among the study groups.

**Discussion**

In the study groups, there were more females than males. This agreed with the results of Graham et al. [16] and Hugon [17], who reported that cognitive symptoms were more frequent in young females than in young males. In



**Fig. 4** Correlation between SPIN-SNR-10 and Oxygen saturation in the study groups (I & II) ( $N=30$ ). SPIN: Speech perception in noise, SNR: Signal to noise ratio

contrast, this finding disagreed with that of Garg et al. [17], who reported that no difference had been observed between males and females in the likelihood of developing cognitive symptoms after COVID-19.

According to the results of the CAP questionnaire for adults in the study groups, 15 subjects (50%) complained of memory problems, ten subjects (33.3%) complained of lack of attention, nine subjects (30%) complained of difficulty in understanding speech in noise, five subjects (16.7%) complained of asking a lot to repeat speech addressed, two subjects (6.7%) complained of other medical problems, two subjects (6.7%) complained of family history of similar conditions, one subject (3.3%) complained of difficulty in sound localization, and one subject (3.3%) complained of work problems. The results of difficulty in concentration and lack of attention agreed with the results of Roger et al. [18]. They reported that these symptoms were present in 19.9% of their patients after recovery. In comparison, the result of memory agreed with that of Davis et al. [19].

In this study, the SPIN test was used to assess Selective Attention (Auditory Figure Ground ability) and Monaural Separation. Post-COVID-19 patients performed statistically significantly worse than the controls at 0 dB S/N and at -10 dB S/N. The post-COVID-19 complaining group (I) performed worse than the post-COVID-19 non-complaining group (II) regarding SPIN-SNR<sup>-10</sup> (Table 2). This result agreed with that of Boboshko et al. [20]. They reported that impaired speech intelligibility was one of

the most frequent auditory complaints in those patients. Those authors speculated that the deterioration of speech test scores in patients after COVID-19 might occur due to auditory processing disorders (APD), memory impairment or changes in cognitive status in general.

Cognitive abilities, along with peripheral hearing and CAP, are known to influence speech intelligibility [21]. The results of speech in noise tests might suggest temporal lobe affection (auditory cortex), which is responsible for selective attention [22]. On the other hand, the results of this study disagreed with the results of Tufatulin et al. [3]. These authors reported that no CAPD was detected in children after the new coronavirus infection. The discrepancy between the results of the current work and that study could be related to the different ages of participants in both studies. They studied children up to the age of 17 years. The retained neuroplasticity in children might play a role in the presence of a discrepancy between the two studies. The few available studies about the evaluation the central auditory abilities in post-COVID-19 adult patients include only Boboshko et al. [20] up to the knowledge of the authors of the current work.

Duration Pattern Sequence test (DP) evaluates temporal ordering, pattern recognition, auditory memory and duration discrimination [13]. Post-COVID-19 patients performed worse than the controls in the DP test. Moreover, the post-COVID-19 complaining group (I) performed worse than the post-COVID-19

**Table 2** Comparison of Speech Perception in Noise Test (SPIN) and Duration Pattern Sequence Test (DPT) across studied groups

Central auditory Test	Group	Range	Mean ± SD	F	P- value		
SPIN 0 dB S/N	Post COVID-19 complaining group (I)	76 – 88	81.30 ± 3.77	116.56	< 0.001*	P1	0.074
	Post COVID-19 non-complaining group (II)	76 – 88	83.20 ± 2.78			P2	< 0.001*
	Control	88 – 96	91.60 ± 2.53			P3	< 0.001*
SPIN -10 dB S/N	Post COVID-19 complaining group (I)	24—36	30.50 ± 4.01	29.13	< 0.001*	P1	0.005*
	Post COVID-19 non-complaining group (II)	24—40	35.00 ± 4.07			P2	0.009*
	Control	32—60	39.20 ± 6.35			P3	< 0.001*
DP sequence Test	Post COVID-19 complaining group (I)	60 – 100	84.63 ± 11.05	22.57	< 0.001*	P1	0.027*
	Post COVID-19 non-complaining group (II)	80 – 100	90.50 ± 7.93			P2	0.014*
	Control	90 – 100	96.88 ± 3.52			P3	< 0.001*

Speech Perception in Noise Test (SPIN) and Duration Pattern sequence Test (DPT), signal to noise ratio (S/N). **P1**: post COVID-19 complaining versus post COVID-19 non-complaining, **P2**: post COVID-19 non-complaining versus control group, **P3**: post COVID-19 complaining versus control group

\* P value is significant at the 0.05 level.  $P \leq 0.05$  significant  $P \leq 0.001$  highly significant

non-complaining group (II) (Table 2). These results may be explained and supported by the results of the Douaud et al. [23] study. These authors analyzed MRIs (structural and functional brain scans before and after COVID-19 infection) of adult subjects who had normal, pre-pandemic MRIs on record at England’s Biobank. Imaging studies revealed the involvement of the left parahippocampal gyrus and anterior parahippocampal gyrus. These two areas are known to play crucial roles in the memory of events (Temporal order of episodic memory) [23–25].

Gap In Noise test assesses temporal resolution ability. It is sensitive to cortical disorders [21]. In this study, the post-COVID-19 patients performed worse than the controls regarding GIN score and GIN threshold. Moreover, the post-COVID-19 complaining group (I) performed worse than the post-COVID-19 non-complaining group (II) with regard to the GIN threshold only (Table 3). This result agreed with that of Boboshko et al. [20]. The authors used the Random Gap Detection Test (RGDT) to evaluate the temporal resolution of the human auditory system in post-COVID-19 patients and reported poor

results of the RGDT in many patients during the post-COVID-19 period.

As regards the Memory Test, the post-COVID-19 patients performed worse than the controls in terms of MR, MC, and MS. Moreover, the post-COVID-19 complaining group (I) performed worse than the post-COVID-19 non-complaining group (II) regarding MC and MS only (Table 4). These results agreed with the results of Graham et al. [16]. The authors reported that long-term COVID-19 patients had significantly worse attention, working memory function and short-term memory. The results of the current work also agreed with the results of Ferrucci et al. [26]. These authors reported that post-COVID-19 patients performed worse on verbal memory tests. Twenty percent of their post-COVID-19 patients showed long-term verbal and spatial memory dysfunctions. Moreover, Douaud et al. [23] identified consistent abnormalities in MRIs of COVID-19 adults in the left parahippocampal gyrus, which is a limbic region of the brain involved in supporting memory of events.

In order to explain the results of the post-COVID-19 non-complaining group, Woo et al. [9] reported that

**Table 3** Comparison of Gap in Noise Test (score and threshold / msec) among studied groups

GIN Test	Group	Range	Mean ± SD	F	P- value		
% score	Post COVID-19 complaining group (I)	53—83	66.69 ± 6.75	91.14	< 0.001*	P1	0.153
	Post COVID-19 non-complaining group (II)	63—75	69.55 ± 3.97			P2	< 0.001*
	Control	75—93	82.85 ± 4.88			P3	< 0.001*
Threshold in msec	Post COVID-19 complaining group (I)	4—8	5.80 ± 1.13	41.40	< 0.001*	P1	0.042*
	Post COVID-19 non-complaining group (II)	4—6	5.20 ± 0.61			P2	< 0.001*
	Control	3—5	4.00 ± 0.71			P3	< 0.001*

Gap in Noise Test (GIN)

**P1**: post COVID-19 complaining versus post COVID-19 non-complaining, **P2**: post COVID-19 non-complaining versus control group, **P3**: post COVID-19 complaining versus control group

\* P value is significant at the 0.05 level.  $P \leq 0.05$  significant  $P \leq 0.001$  highly significant

**Table 4** Comparison of Auditory Memory Test among studied groups

Variable	Group	Range	Mean $\pm$ SD	F	P-value		
Recognition memory	Post COVID-19 complaining group (I)	73 – 100	92.72 $\pm$ 8.56	3.355	0.044*	P1	1.00
	Post COVID-19 non-complaining group (II)	73 – 100	92.72 $\pm$ 9.39			P2	0.142
	Control	91 – 100	98.18 $\pm$ 3.73			P3	0.047*
Memory for content	Post COVID-19 complaining group (I)	5 – 7	6.25 $\pm$ 0.55	73.116	< 0.001*	P1	< 0.001*
	Post COVID-19 non-complaining group (II)	6 – 8	7.20 $\pm$ 0.78			P2	< 0.001*
	Control	8 – 9	8.50 $\pm$ 0.51			P3	< 0.001*
Memory for sequence	Post COVID-19 complaining group (I)	4 – 6	5.30 $\pm$ 0.57	70.324	< 0.001*	P1	0.029*
	Post COVID-19 non-complaining group (II)	5 – 7	5.90 $\pm$ 0.73			P2	< 0.001*
	Control	7 – 8	7.45 $\pm$ 0.51			P3	< 0.001*

**P1:** post COVID-19 complaining versus post COVID-19 non-complaining, **P2:** post COVID-19 non-complaining versus control group, **P3:** post COVID-19 complaining versus control group. \*:P value is significant at the 0.05 level.  $P \leq 0.05$  significant  $P \leq 0.001$  highly significant

subtle cognitive deficits would not restrain most patients in daily life and were only unmasked by specific screening tests. These cognitive deficits include deficits in short-term memory, attention and concentration.

Douaud et al. [23] reported that there was a greater loss of gray matter in several areas of the COVID-19 brains in their MRIs. These areas include the left parahippocampal gyrus, cingulate cortex, insula, hippocampus, limbic cortical areas, amygdala and temporal pole. Many of the areas are related to auditory working memory, recall and language [27, 28]. The insula is important for understanding speech in noise, dichotic listening, temporal processing and auditory attention [29].

There are several different mechanisms involved in COVID-19-associated CNS dysfunction. These include direct viral effects (olfactory pathway or across the blood–brain barrier) and indirect mechanisms (hypoxia, activation of the immune system, inflammatory and thrombotic pathways) [30, 31]. COVID-19 was proven to spread through the olfactory epithelium and the ethmoid bone to the olfactory bulbs in the brain, causing olfactory disorders along with memory impairment and cognitive disabilities [32]. It is reported that COVID-19 has a known neurotropism [30].

The central auditory pathways are hypothesized to be damaged by inflammation, leading to APD later [20]. Inflammatory factors have been shown to not return to normal status months after recovery [33]. Chronic systemic inflammation after COVID-19 infection exacerbates neurodegeneration. Thus, potentially, this would lead to long-term cognitive deficits [34].

Silent strokes or lack of oxygen also could damage the COVID-19 patient's brain. Silent strokes typically affect the brain's white matter — the wiring between brain cells that enables different parts of the brain to communicate with each other. This wiring is essential for attention, and when it is damaged, sustained attention is impaired [10].

Ferrucci et al. [26] reported that the memory impairments observed in patients with COVID-19 months after hospital discharge could be related to hypoxic factors. Long-lasting hypoxia might contribute substantially to post-infection cognitive impairments. This is because neurons are sensitive to hypoxic injury [35].

Moreover, Selective neuronal mitochondrial targeting in COVID-19 infection could affect cognitive processes. Hypoxia of brain areas may increase the reproductive capacity of the virus. In areas of cerebral hypoxia, neuronal cell energy metabolism may become compromised after the integration of the viral genome, resulting in mitochondrial dysfunction. Accordingly, neurons would become dysfunctional [8].

Furthermore, the prolonged immune response can lead to post-COVID-19 sequelae. This mechanism has the potential to cross the blood–brain barrier and affect neural regions and function, including cognition [36]. This mechanism or hypothesis is supported by the results of Graham et al. [16] work. These authors reported that the female: male ratio of 2.3:1 was reminiscent of autoimmune diseases.

A statistically significant positive correlation was revealed between the GIN score and the time between attacks and testing (weeks). The longer the interval between the attack and the test was, the better the GIN score was. This result agreed with the results of Davis et al. [19]. Those authors reported that systemic and neurological/cognitive symptoms were the most likely to persist from disease onset to seven months. In contrast, the onset of brain fog/cognitive dysfunction occurred in the first week of symptoms. Reports of cognitive dysfunction increased over the first three months and then decreased slightly in the following months. This change might be linked to the decrease of antibody levels with time [37].

Moreover, there was a statistically significant positive correlation between the results of SPIN-SNR<sup>-10</sup> (test of

attention) and O<sup>2</sup>-saturation. This result can be explained by the results of Areza-Fegyveres et al.'s [38] work. They reported that patients with chronic hypoxia might have the worst performance on attention tests. Also, Almeria et al. [30] reported that the need for oxygen therapy in COVID-19 patients was associated with memory, attention and executive function deficits.

## Conclusions

The most common post-COVID-19 central auditory affected symptoms included memory problems, lack of attention, difficulty in understanding speech in noise and difficulty in concentration. There was affection of attention on post-COVID-19 patients who suffered from decreasing O<sup>2</sup> saturation during the attack. CAT results were statistically significantly worse in post-COVID-19 patients than in healthy subjects. Also, CAT results were significantly worse in post-COVID-19 complaining patients than in post-COVID-19 non-complaining patients. Non-complaining post-COVID-19 subjects still had affected scores relative to the control group regarding memory and the GIN test. Thus, Memory tests and GIN tests should be used for screening in post-COVID-19 patients even if they have not complained of any central auditory system symptoms.

## Abbreviations

ACE2	Angiotensin-converting enzyme 2
(c)APD	Central auditory processing disorders
CATs	Central Auditory Tests
COVID-19	Corona virus disease 2019
DPT	Duration Pattern Sequence Test
GIN	Gap in Noise Test
HCoV	Human coronaviruses
one-way ANOVA	One-way Analysis of variances
S/N	Signal to noise ratio
SPIN	Speech Perception in Noise Test

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none.

## Authors' contributions

Conceptualization: EK. Data curation: SH, EK, AE, NN, Formal analysis: SH, EK, AE, NN, Methodology: SH, EK, AE, NN,. Writing – original draft: SH. Writing – review & editing: SH, EK, AE, NN.

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## Availability of data and material

All data generated or analyzed during this study are included in this article. Further enquiries can be directed to the corresponding author.

## Declarations

### Ethics approval and consent to participate

Study statement Approval:

- This study was approved by the Tanta University Research Ethics Committee with approval code number (34932/9/21).
- Consent to participate statement: A written informed consent was taken from each subject in this study after explaining all the tests in compliance with the Helsinki Declaration.

### Consent for publication

Not applicable.

### Competing interests

The authors declare that they have no competing interests.

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