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The Impact of COVID-19 on Auditory and Visual Choice Reaction Time of Non-hospitalized Patients: An Observational Study

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ABSTRACT

Background and aim: COVID-19 is a multi-system infectious disease. There is accumulating evidence showing the damage caused by the virus on a nervous system other than the lungs. It is still unknown whether this Central nervous system (CNS) complications are reversible. Reaction time indicates neuronal activity, and an increase in RT denotes defective neural function. Hence the present study was done to measure the impact of COVID-19 on auditory and visual reaction time during COVID-19 disease, four and eight weeks after recovery.

Material and methods: ART and VRT were measured using discriminatory and choice reaction time apparatus. Results were analyzed using an unpaired t-test. The study involved 86 participants of both genders aged 21-40. Forty-six were acute, mild COVID-19 positive patients and 40 were healthy (control) subjects.

Results: During COVID-19 disease, a statistically significant increase in visual reaction time (VRT) values for both green and red colours ($p<0.001$) and ART ($p<0.001$) were observed in the study group when compared with the control group. After 4 weeks of recovery, a significant increase in VRT ($p<0.05$) for both the colours and ART ($p<0.05$) were observed compared with control, but the values were lesser when compared with during COVID-19 disease in the study group. After 8 weeks, no statistically significant difference ($p>0.2$) was observed between both groups. No gender difference was detected.

Conclusions: Increased RT values indicate that COVID-19 affects the nervous system. The decline in RT values after 4 weeks and normal values after 8 weeks of recovery shows improvement in nerve function.

1. Introduction

The damage caused by COVID-19 infection (SARS-CoV-2) on the lungs is quite known. However, studies show the extension of this virus beyond the respiratory system, including the cardiovascular system, gastrointestinal system, renal system, and nervous system. Per recent studies,36.4% of patients with COVID-19 (especially severely affected individuals) had neurological symptoms, posing a significant risk of morbidity and mortality.[1] The commonly reported symptoms include headache, disturbed consciousness, paresthesia, loss of smell, taste and vision, partial neuronal degeneration, and brain tissue edema.[2] The common neurological manifestations during and after COVID-19 include encephalopathy, encephalitis, meningitis, acute cerebrovascular disease, and Guillain-Barre syndrome.[3] Reaction time (RT) measures the quickness with which a response occurs. It is the interval between the presentation of the stimulus and the motor response. Reaction time needs an intact sensory system, cognitive processing, and motor performance.[4] The stimulus could be auditory, visual, tactile. Factors affecting reaction time include gender, age, physical fitness, level of fatigue, distraction, alcohol, personality type, limb used for the test, and biological rhythm. Three basic reaction time paradigms have been described: (1) simple reaction time has a single stimulus and a single predefined response, (2) recognition reaction time has several false stimuli mixed with one correct stimulus prompting the response, and (3) choice reaction time involves multiple stimuli and differing responses for each stimulus.[5] In the present study, Choice reaction time was used as it has high test-retest reliability and also activated more brain areas. Choice reaction time studied using visual inputs is known as visual choice reaction time (VRT), and auditory inputs are known as auditory choice reaction time.

RT response will be faster with an intact nervous system. Faster RT also indicates better cognitive functioning, including memory, verbal fluency, and intelligence.[6] RT has an important role in day-to-day activities, from responding to a doorbell, answering MCQs on the internet, driving. Damage to the nervous system can impair these daily activities. The accepted values

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for the simple reaction time are 180-200 ms for light stimuli and 140-160 ms for sound stimuli.[7] It is unknown whether this injury to the nervous system is transient or persistent. Assessing reaction time is an indirect, non-invasive and simple way of examining the integrity of central and peripheral nervous systems. Hence the present study aims to determine the effect of COVID-19 on audiovisual reaction time in affected individuals during illness and after one and two months of recovery.

Objectives:

1. To measure the impact of COVID-19 on auditory and visual reaction time during COVID-19 illness.
2. To measure the impact of COVID-19 on auditory and visual reaction time four and eight weeks after recovery from the disease.
3. To measure the auditory and visual reaction time in healthy non-COVID-19 subjects.
4. To compare and analyze the auditory and visual reaction time values during and after 4, 8 weeks of COVID-19 patients with the control.

2. Material and methods

This observational, cross-sectional study was done in the Department of Physiology of a private medical college and in a district hospital between July - October 2021 with a study population of 86, of which 46 were COVID-19 positive (study) patients and 40 were non-COVID-19, healthy (control) subjects. The study was done using a non-probability sampling technique. Volunteered patients from the department of General medicine were included in the study. The study was conducted after obtaining Institutional ethical clearance (IEC no: VMCIEC/88/2021). Informed written consent was obtained from each participant. The purpose of the study was explained to them in the language they could comprehend. The confidentiality of the participants was ensured, and they were informed that they could withdraw from participating in the study anytime. RT-PCR COVID-19 positive subjects in the age group between 20 to 40 years of both the genders and with BMI between 22.3-25.3 were included in the study. Only mild COVID cases (score 0-4) as categorized by the disease severity classification system for COVID-19, Republic of Korea (Bulletin of World Health Organization) were included in the study. This classification is based on the pulse rate, systolic blood pressure, respiratory rate, body temperature and level of consciousness.[8] According to this, moderate cases had a total score of 5–6, and severe and very severe cases had a score $\geqslant 7$.

For the control group, healthy subjects aged 20 to 40 years of both genders were included. Subjects with diabetes, visual defects, ENT disorders, cardiovascular and respiratory diseases, psychiatric disorders, neurological disorders, cataracts, on drugs, smoking, and alcoholism were excluded from the study. Baseline data on all participants were collected using a structured questionnaire. All the participants were instructed to refrain from caffeine, smoke for 12 hours and have an adequate sleep before the day of testing. Weight was measured with an electronic weighing scale (Doctor Beliram and sons, New Delhi) and height with a stadiometer. VRT for green and red light and ART was measured with the help of discriminatory and choice reaction time apparatus (Anand Agencies, Pune). The study was conducted between 10-12 pm every day to evade the effects of the circadian rhythm. The same COVID-19 patients were followed-up after 4 and 8 weeks of recovery.

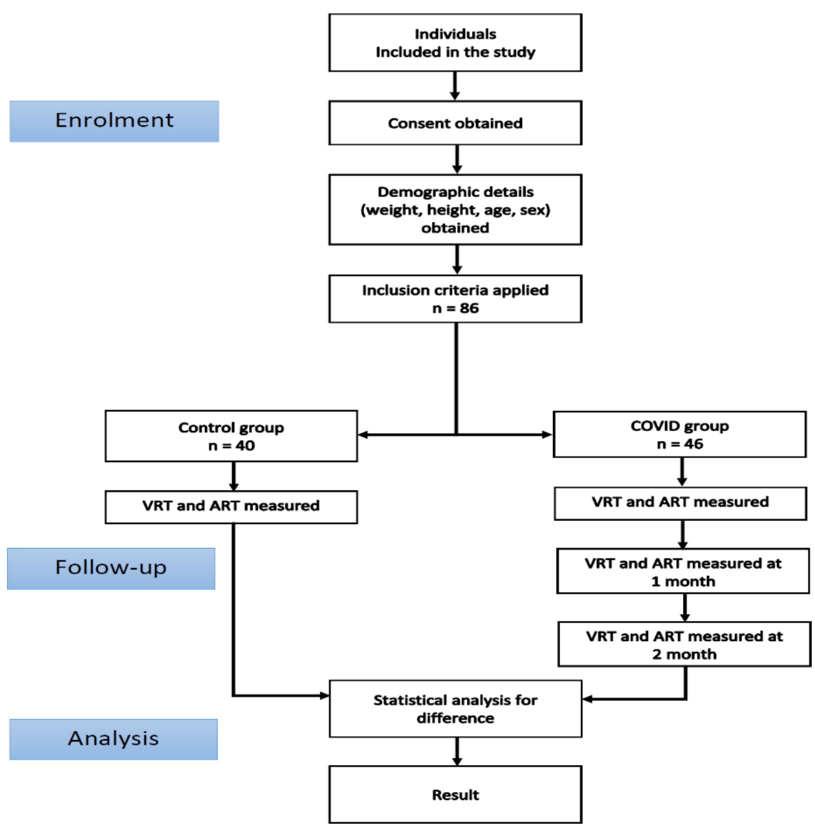

Fig. 1. Methodology flow chart.

Visual Reaction Time (VRT) and Auditory Reaction Time (ART) second were measured in the sitting posture in a quiet room with an accuracy of 0.001. The visual stimulus was provided by red and green light, and a beep sound provided the auditory stimulus. The subject was initially instructed about the complete procedure to record the baseline VRT for the green light. The subject should keep pressing the index finger of the right hand on the response button, and once he visualizes the stimulus, he immediately has to remove his finger. The response button terminated the clock counter and the value of VRT in milliseconds was displayed on the screen. Sufficient time was given for the participants to thoroughly get acquainted with the procedure. After the practice trial, three readings were taken once the patient felt comfortable, and the fastest response value was taken as the final reaction time. Baseline VRT for a red light was also recorded similarly. The same procedure was followed to collect the values in all COVID-19 subjects after 1 and 2 months. Proper COVID-19 guidelines were followed in handling COVID-19 patients, and the instruments used were sterilized every time before taking each value. For ART, after giving tone stimuli in the same apparatus, the subject was asked to release the key, which gave the ART value in milliseconds. Similarly, VRT and ART were recorded in control subjects also.

3. Results

Statistics analysis

The data was entered in MS Excel and analyzed using SPSS 24. The readings of AV reaction time during COVID-19 disease and after one and two months of recovery were analyzed and compared with the control group using an unpaired t-test. P-value less than 0.05 was the cut-off to determine statistical significance.

Table 1. Demographic and anthropometric details of the study (case) and control groups.

		Groups		P-value
		Control (40)	Case (46)	
Gender %	Male	12 (30%)	16 (35%)	0.402
	Female	28 (70%)	30 (65%)	
Age in years (mean±SD)		31.2±4.9	31.4±6.4	0.438
Range(years)		22-40	21-40	-----
BMI (mean±SD)		24.3±0.6	24.4±0.81	0.161
Range		22.6-25.2	22.3-25.3	-----

Table 2. Visual reaction time for green and red colour stimuli in the study versus control group during and after 4 and 8 weeks of recovery from COVID-19.

Mean ± SD	Control	COVID-19 0 week(during illness)	COVID-19 post four weeks	COVID-19 post eight weeks
Green	170.80±22.71	202.63±29.23	181.4±21.9	173.33±20.07
Red	161.92±21.79	201.46±26.08	181.93±21.52	164.50±17.55
P-value	-----	p<0.001*	p<0.05*	p>0.2

* Statistically significant

According to Table 2, during COVID disease, VRT values for green and red colour were significantly higher ($p<0.001$) in the study group than in the control group, indicating a delay in nerve conduction. After four weeks of recovery, there was a decrease in the mean VRT values of the study group, but a statistically significant increase ($p<0.05$) was observed compared with the control group. It shows that the nerve function has started improving. After eight weeks, complete recovery was noticed as no statistically significant difference ($p>0.2$) was observed between the study and the control group.

Table 3. Auditory reaction time in the study versus control group during and after 4 and 8 weeks of recovery from COVID-19.

Mean ± SD	Control	COVID-19 0 week(during illness)	COVID-19 post four weeks	COVID-19 post eight weeks
Tone stimulus	152.86±29.76	176.78±21.66	161.98±17.7	155.85±15.49
P-value	-----	p<0.001*	p<0.05*	p>0.2

* Statistically significant

According to Table 3, during COVID-19 disease, ART values were significantly higher ($p<0.001$) in the study group than in the control group indicating damage to the brain and the nervous system. After four weeks of recovery, though a statistically significant increase ($p<0.05$) was observed in the study group compared with the control group, mean ART values of the study group were lesser than during COVID-19 disease. This shows that the nerve function has started improving. After eight weeks, no statistically significant difference ($p>0.2$) was observed between the study and the control group showing marked improvement in nerve function.

Table 4. Gender differences in auditory and visual reaction time.

	Female VRT (Green)	Male VRT (Green)	Female VRT (Red)	Male VRT (Red)	Female ART	Male ART
Mean	200.3	207.1	200.1	204.0	178.1	174.3
SD	26.9	33.6	22.6	32.4	20.3	24.6
P-value	0.23		0.32		0.29	

According to Table 4, no statistically significant differences in ART and VRT values were observed between males and females.

4. Discussion

During COVID-19 disease, a statistically significant increase in VRT values for green and red colour ($p<0.001$) and ART ($p<0.001$) were observed in the study group when compared with the control group (Table 2). An increase in reaction time values indicates that more time is taken for conduction in sensory-motor pathways. This could be due to the nervous system damage caused by the COVID-19 disease. The present study results agree with previous studies on patients with brain diseases, where RT was found to be slower, especially in subjects with lesions in the left cerebral hemisphere.[9, 10] The slower reaction time indicates delayed neuronal activity.[11] Though the virus is detected in the CSF of infected patients, previous studies on COVID-19 had shown that the nervous system involvement could be due to widespread malfunction of the immune system and dysregulation of blood vessels rather than the direct entry of the virus into the brain.[12] Ischemic and demyelinating changes are seen in the cerebrum, cerebellum and hippocampus neurons in COVID-19 patients.[13] The presence of myelin sheath helps in faster conduction of impulses from one node to another node, as myelin insulates the axon and assembles voltage-gated sodium channels in the nodes of Ranvier. Demyelination slows down the conduction velocity along sensory and motor nerves prolonging RT.[14] The commonest symptoms of COVID-19 include headache, loss of smell, dizziness and loss of taste.[15] Emerging studies show that all nervous system components are affected, including central, peripheral, and muscular. In the present study, frequent CNS and PNS symptoms encountered in patients with mild COVID-19 infection were myalgia (67.4%), loss of appetite (34.8%), headache (17.4%), loss of smell (17.4%), and loss of taste (15.2%). Other non-specific symptoms include fever, cough, fatigue, and dyspnoea. In both the control and the study group, ART was lesser (faster) than VRT (Table 2 and 3). Two reasons could explain this. One is that males' temporal lobe is more well-developed than the occipital lobe and the second reason is the presence of multiple synapses in the visual (20-40ms) than in the auditory (8-10ms) pathway.[16] Normally males have a faster RT when compared to females due to stronger motor performance.[7] Slower RT in females might be due to estrogen and acetylcholine synthesis resulting in delayed nerve conduction. However, no such significant difference was present statistically in the present study, though mean VRT values are slightly more in males (Table 4).[17] Also, in the present study, the reaction time for red is a little faster than green in both the control and the study groups. This is in agreement with the previous studies conducted on VRT for different colours.[18] Sudden onset sensorineural hearing loss was also reported after COVID-19.[19] Reports as well had shown that mild acute COVID-19 patients who were never hospitalized had persistent neurological symptoms (long haulers), and no correlation was observed between disease onset and recovery time.[20, 21] In the present study, we also checked using AVRT whether the neurological issues were lasting after four and 8weeks of clinical recovery. It was observed that after four weeks of recovery from illness, reaction times were still prolonged when compared with the control (Table 2 and 3). However, the values in the study group were lesser than those during COVID-19 disease. This is an indication that the nerve function is improving. After eight weeks of COVID-19 recovery, the reaction time values in the study group were almost equal with the control group, showing the immense improvement in nerve function in two months. This was the first study to observe the neurological recovery in post-COVID-19 patients using the audiovisual reaction time.

Limitations of study

A larger sample size including not only mild, non hospitalized patients but also moderate and severely ill patients is needed to reach more accurate information. The study could have been extended for a few more months to obtain a complete recovery. Advanced neuroimaging techniques like MRI EMG-NCV were not done to support the findings. The reaction time varies with the phases of the menstrual cycle in females. However, this was not considered in the present study as only a limited number of patients volunteered for the study.

5. Conclusions

The present study results show that both ART and VRT for green and red colour were prolonged during COVID-19 disease. This specifies the involvement of the nervous system in COVID-19 infection irrespective of whether the patients came with neurological or respiratory symptoms. The values of ART and VRT for both the colours gradually decreased over 4 and 8 weeks of recovery, indicating improvement in nervous function. Even then, the ART and VRT values were slightly prolonged compared to the control. These preliminary results are shared to inform that CNS involvement occurs in COVID-19 infection but might gradually resolve in mild cases. Early recognition and prompt treatment of COVID-19 cases are essential to prevent long-term neurological consequences.

Conflict of Interest

The authors declared that there is no conflict of interest.

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