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Attention profile of physically recovered COVID-19 inpatients on the day of discharge

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ABSTRACT

Few studies have reported specific attention deficits in post-COVID-19 patients. Attention consists of different subdomains. Disruptions to specific attention subdomains might impair a wide range of everyday tasks, including road safety. As there are millions of COVID-19 patients with different socio-economic backgrounds, screening of attentional performance less dependent on education is needed. Here, we verified if physically recovered COVID-19 inpatients showed specific attention decrements at discharge. The Continuous Visual Attention Test (CVAT) is a Go/No-go task which is independent of participants' schooling. It detects visuomotor reaction time (RT = intrinsic alertness), variability of reaction time (VRT = sustained attention), omission (focused-attention), and commission errors (response-inhibition). Thirty physically functional COVID-19 inpatients at discharge and 30 non-infected controls underwent the CVAT. A MANCOVA was performed to examine differences between controls and patients, followed by post-hoc ANCOVAs. Then, we identified the percentile score for each patient within the distribution of the CVAT performance of 211 subjects mentally capable of driving (reference group). COVID-19 patients at discharge showed greater RT and VRT, and more omission errors than controls. Twenty-two patients (73%) had performance below the 5th percentile of the reference group in one or more subdomains. As slow visuomotor RT, deficits in focusing and difficulties in keeping visual attention are associated with traffic accidents, we concluded that most COVID-19 patients at discharge had deficits that may increase the risk of road injuries. As these deficits will probably affect other daily activities, a routine assessment with the CVAT could provide useful information on whom to send to post-COVID centers.

1. Introduction

Previous studies in post-COVID-19 patients have shown attention impairments several weeks after discharge (Almeria et al., 2020; Zhou et al., 2020; Mcloughlin et al., 2020; Woo et al., 2020; Boldrini et al., 2021; Hamphire et al., 2021; Ortelli et al., 2021). Attention is not a unitary construct and consists of distinct subdomains (Petersen and Posner, 2012; Egeland and Kovalick-Gran, 2010). Specific attention deficits may affect safety in common daily life activities. In particular, traffic safety has been shown to be compromised when road users have specific difficulties in focusing and keeping visual attention, and when visuomotor reaction-time increases (Brower, 2002; Andersson and Peters, 2019). Road safety is a major public health concern (Global status report on traffic Global status report on road safety, 2018). Indeed, studies conducted before the current pandemic have reported that traffic injuries are the leading cause of death in people aged 5–29 years worldwide (Passmore et al., 2019). As post-COVID-19 patients who are physically fully recuperated at discharge may have specific attention subdomain impairments, they could potentially represent a (transient) safety hazard. Furthermore, the implications of specific attention deficits in post- COVID-19 patients might go beyond traffic safety, as these deficits will likely not only affect driving, but also job and academic performance as well as household activities. However, despite the importance of attention subdomains for cognitive functioning and road safety, there is a lack of studies on subdomain deficits in COVID-19 patients on the discharge day.

Attentional assessments in COVID-19 patients have used various neuropsychological tools, which suffer from some limitations, including

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time to complete the assessment, dependence on multiple functions other than attention or not measuring all attention subdomains, and dependence on educational level. Regarding the first limitation, it is known that traditional and web-based neuropsychological batteries sometimes take a long time to complete. In this regard, continuous performance tests of long duration (i.e., >5 min) have been used in COVID patients (e.g, Zhou et al., 2020). However, at discharge COVID-19 patients may still suffer from fatigue with continuous effort (Ortelli et al., 2021), potentially impairing performance on longer cognitive assessments. Other tests that have been previously used on pen-and-paper and on a tablet, including the Trail Making Test and the Digit-Symbol usually do not take a long time to complete and, thus, performance will suffer less from fatigue. However, such tests do not cover all attention subdomains and do not measure attention alone, but rather depend on multiple functions, such as fine motor control, eye movements, visual scanning, executive functions, and working memory (Lezak, 2012). Tests more focused on attention, such as the D2-test and the Test of Everyday Attention still depend on visual screening and other cognitive functions and take a long time to complete (Lezak, 2012) which increases the likely influence of fatigue on performance. Finally, most of the tests, such as the Digit-Symbol, are influenced by culture or educational level (Lezak, 2012). As there are millions of people with different cultural backgrounds admitted to the hospitals for COVID-19, screenings of the attention subdomains in faster ways and less dependent on culture and education level are needed.

Speed and consistency by which individuals process visual information could provide such a screening tool. Performance on Go/No-Go reaction-time paradigms measures attention based on choosing and concentrating on relevant stimuli. The Continuous Visual Attention Test (CVAT) is a 90-s Go/No-Go test (Schmidt et al., 2020). Previous studies in non-COVID subjects have suggested that the CVAT can be used to identify attention subdomains impairments independent of participants' schooling (Schmidt et al., 2021). The number of correct hits (Go) reflects focused attention, whereas the number of incorrect hits or false alarms (No-Go) indicates response inhibition (Simões et al., 2018). Intrinsic alertness is assessed by measuring average visuomotor reaction times (RT) for the correct hits (Simões et al., 2018). The CVAT also produces intraindividual variability of RT (VRT), which measures the fluctuation in RTs and is associated with sustained attention (Simões et al., 2018).

As the CVAT is easy to administer and gives important information on the attention subdomains (Schmidt and Manhaes, 2019), it is expected that a routine assessment with the CVAT at the discharge day from hospital could give useful evidence on whom to send to post-COVID centers for more comprehensive testing later on. In addition, this short and culture fair attention task would be applicable in any clinic worldwide (Schmidt et al., 2021). Moreover, as the attention subdomains are essentials for higher-order cognitive performance (Lezak, 2012), the CVAT could provide relevant information on the cognitive outcome of inpatients with COVID-19 at the discharge day.

The present investigation aimed to study differences in performance on attention subdomains between controls and COVID-19 inpatients that were physically recuperated at discharge. Then, we investigated the functional implication of the patients' performance focusing on the attention demands required for maintaining road traffic safety. To accomplish this objective, we considered the relative position of each patient's performance within the distribution of the four attention subdomains based on a large sample of subjects who got a valid health certificate for driving and performed the CVAT before the current pandemic.

2. Material and methods

2.1. Participants (patients and controls)

Between April 14th and December 30th, 2020, COVID-19 inpatients were recruited from a tertiary university hospital in Rio de Janeiro, Brazil. All patients had a SARS-CoV-2 infection confirmed by a positive PCR from nasopharyngeal swab. The control group is part of another study (van Duinkerken et al., 2021) and were evaluated at the same hospital between May 14th and July 1st, 2020. The control group consisted of age- and sex-matched hospital workers who had not had a previous infection with SARS-CoV-2, and who were not in direct contact with COVID-19 patients before the CVAT assessment.

The general exclusion criteria for the two groups were as follows: age >70 or <18 years; taking antipsychotic or anti-epileptic medication at any time, and psychotropic drugs that could interfere with attention performance; reduced kidney or hepatic function; past head trauma and loss of consciousness; current alcohol/substance use disorder; pre-existing neurologic or psychiatric disorders; non-corrected hearing or visual impairments; and previous cognitive impairment. We also excluded patients that during hospitalization showed one or more of the following conditions: delirium, new neurological symptoms, or orotracheal intubation.

The participation was voluntary, and the research protocol was approved by the local ethical committee (CAA: 30547720.3.0000.0008). The study was performed in accordance with the Helsinki Declaration. Informed written consent was obtained from the participants.

2.2. Procedures

Patients admitted to the hospital were assessed two times per day for level of consciousness and only those who had been alert and calm were included. They presented a Richmond Agitation Sedation Scale = 0 (Sessler et al., 2002) during hospitalization. Criteria for discharge were a minimum oxygen saturation of 94% in ambient air without oxygen supplementation for the last 24 h. Additionally, we included only patients who had recuperated physical functionality at discharge. The functional status of COVD-19 inpatients on the day of discharge was assessed by the physician on duty at that day. The patient should be able to eat, walk, and use a toilet without assistance.

For the included patients, the CVAT (Schmidt and Manhaes, 2019) was administered on the day of discharge. The corresponding controls were evaluated at the same hospital during the pandemic. CVAT (Fig. 1).

Subjects were seated in front of a computer. The distance between the center of the monitor and the eyes was approximately 50 cm. The examiner instructed the subject to press the spacebar on the keyboard as fast as possible each time a specific target was displayed. The test started with instructions and a practice session. The practice sessions took 10 s. A second practice session was administered if the participant failed the first one. Only participants who succeeded in the practice session (first or second) were allowed to continue the experiment. In the present study all the participants did not fail the practice tasks. The main task consisted of 90 trials (two figures presented, one each time, target or non-target), 72 correct targets and 18 non-targets. The interstimulus time interval was 1 s. Each stimulus was displayed for 250 ms. The test took 1.5 min to complete. The types of measures included omission errors (focused attention), commission errors (response inhibition), average reaction time of correct responses (RT; intrinsic alertness), and variability of correct reaction times (VRT, sustained attention). VRT was estimated by a per-person measure of the standard deviation (SD) of individual RTs for the correctly signaled targets. To exclude the possibility that a participant's VRT might be related to RT, we calculated the coefficient of variability (CV=VRT/RT). The participants had to reach more than 50% of the total correct hits (minimum number of correct RT measurements per participant = 37). Previous studies have shown that RT and VRT can be reliably measured by tests as short as 52 s with 20 items (Manuel et al., 2019). In the present study one participant (COVID-19 group) made 39 omissions errors and was excluded from analysis.

Fig. 1. Schematic overview of the CVAT showing the target (star) and non-target (diamond). The CVAT begins with written instructions on the screen (A): "In this test, the computer alternately displays the indicated figures in the center of the screen. You must press the spacebar using your dominant hand as fast as you can whenever the star appears in the center of the screen. If the other figure appears, you should not press the space bar." The target (B) remains on the screen for 250 ms (ms). The non-target (C) also remains on the screen for 250 ms. The test consisted of 90 trials (two figures presented, one each time, whether targets or not). The interstimulus time interval was 1 s. The total test took 1.5 min to complete. Variables: omission errors, commission errors, average Reaction Time of the correct responses (RT), and Intraindividual Variability of Reaction Time (standard deviation of the RTs during the test). The CVAT is open for research and for clinical use for licensed psychologists, upon request to Prof. Sergio L. Schmidt (corresponding author). There are versions in English, Spanish, and Portuguese. CVAT: Continuous Visual Attention Test. (Schmidt and Manhães, 2019).

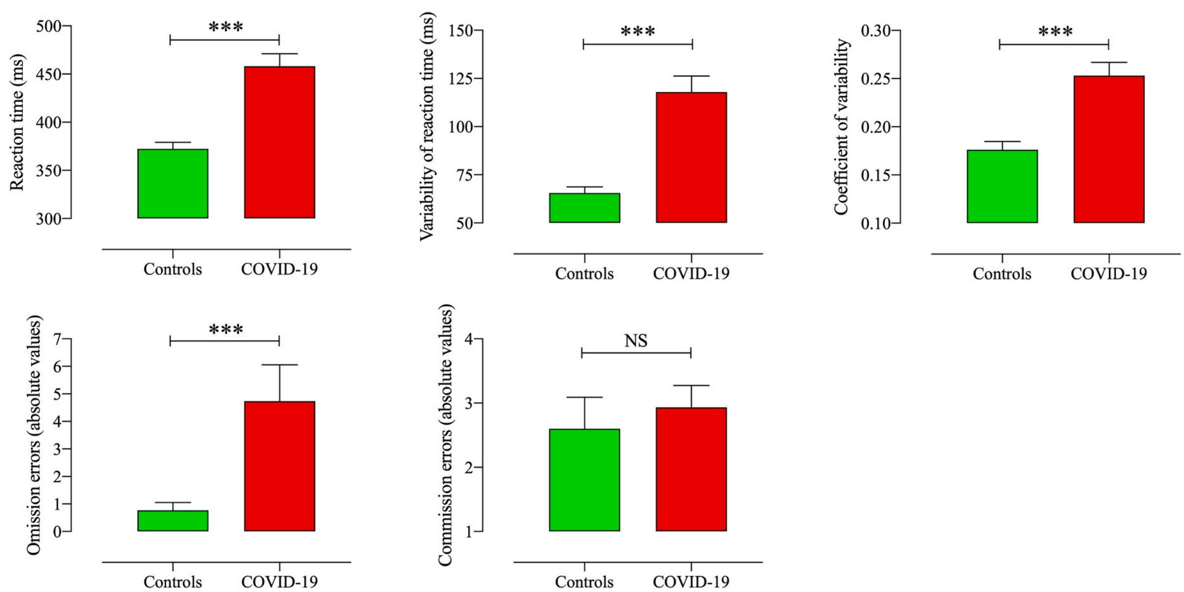

Fig. 2. Bar graph of the mean with standard error of the mean (vertical line) of the CVAT variables. Green bars represent controls who performed the test at the hospital during the pandemic. Red bars denote those who underwent the CVAT on the day of discharge from the hospital, after being admitted with a confirmed COVID-19 infection. Note the significant effect of COVID-19 on all the variables of the CVAT except for commission errors. The effect of COVID-19 on the Coefficient of Variability (VRT/RT) indicates that the increase in the variability of reaction time (VRT) is, at least in part, independent of the Reaction Time (RT). *** = P < .001; NS = non-significant; ms = milliseconds; CVAT: Continuous Visual Attention Test.

2.3. Reference group (subjects deemed mentally capable of driving assessed before the pandemic)

This group was selected based on a subsample of subjects taking a mandatory medical and psychological exam for a certificate of fitness to drive between June and December 2019. The subjects performed their mandatory exams with Brazilian registered medical and psychological practitioners. All subjects taking the mandatory exam were invited to participate in a large national study on CVAT performance. Those who agreed to participate performed the CVAT on the same day and at the same place of the mandatory health exam.

We included in the reference group all the approved subjects who fulfilled the general inclusion criteria for both the controls and the COVID-19 patients of the present study (n = 211). The subjects approved in the mandatory test had a normal neurological exam, absence of visual and hearing impairments, and a mini-mental status examination in the normal range after adjusting for the educational level. Psychological performance was always greater than the 25% percentile of the general population on psychometric validated instruments assessing IQ, global attention, and memory.

2.4. Statistical analysis

Demographic variables were analyzed using independent sample t-tests for normally distributed continuous variables or chi-square tests for categorical variables. All the following statistical procedures were performed using the dependent variables (omission errors, commission errors, RT, and VRT). Statistical procedures were also performed, replacing VRT and RT with CV.

To assess the effect of COVID-19 on attention subdomains, a MANCOVA was performed to examine group differences (COVID-19 vs. controls) for the CVAT variables, using age, sex, and educational level as covariates. In case of a significant overall MANCOVA, post-hoc ANCOVAs for each dependent variable were checked for statistical

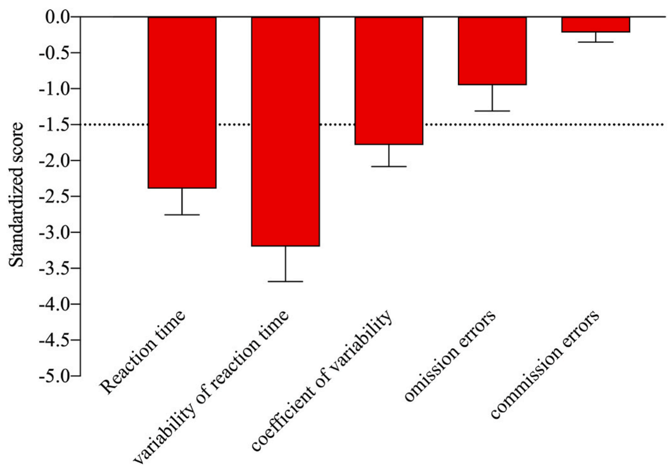

Fig. 3. Bar graph of mean standardized score and respective standard error of the mean (vertical line) of COVID-19 patients for each CVAT variable. For each CVAT variable, the scores were created based on the means and standard deviations of the control group. Thus, the controls have a mean of 0 and a standard deviation of 1, representing the x-axis. As the standardized scores are dimensionless, it is possible to compare the effect of COVID-19 on the different variables of the CVAT. Shown in red are the mean standardized scores for the group who were hospitalized for a COVID-19 infection and assessed on the day of discharge from the hospital. Negative values indicate a worse performance as compared to controls. The dashed line indicates the usual cutoff value. Note that the mean standardized scores for reaction time (RT) and variability of reaction time (VRT) are below the dashed line. The same is observed for the coefficient of variability (VRT/RT). Note that VRT is the most affected variable followed by RT. As the coefficient of variability (VRT/RT) is also affected, VRT deficits are partially independent of RT. The mean standardized score of the omission error variable approaches to the cutoff value. The commission error variable is not affected. CVAT= Continuous Visual Attention Test.

significance. For the MANCOVA and each of the ANCOVAs, the η2 (Eta-squared) was computed to calculate the effect size of the results. Cohen has suggested that $\eta 2 = 0.01$ should be considered a small effect size, 0.06 a medium effect size, and 0.14 a large effect size (Cohen, 1988).

Direct comparisons of the effect of COVID-19 on the different variables of the CVAT were done using standardized non-dimensional scores calculated using the means and the standard deviations of the control group for each CVAT variable. This score showed how many standard deviations a particular patient was above or below the control group mean. We calculated the mean score of the patients for each CVAT variable and considered a mean score below −1.5 SD as a cut-off for meaningful differences between the groups.

To investigate relevant attentional deficits in COVID-19 patients, we calculated the percentiles of the frequency distributions for each CVAT variable considering the data from the reference group, according to five age ranges (20–29, 30–39; 40–49, 50–59, and 60–69 years). For each CVAT variable, a participant's performance equal to or less than the 5th percentile based on the reference group was classified as being significantly impaired. All individuals in the reference group are deemed mentally capable of driving, regardless of their percentile on the CVAT. Therefore, the choice of the 5th percentile of the reference group represents the error to consider a participant (control or patient) as abnormal (error = 5%) when she (he) is normal. Differences between the number of impaired controls and patients were tested with chi-square tests.

For all the tests, significance was set at p-value < .05 (bilateral).

3. Results

3.1. Demographics (Table 1)

After applying the exclusion and inclusion criteria, 30 patients and their respective age and sex-matched controls were selected. There were no statistically significant group differences among the demographic variables, except for educational level, which was higher in the control group compared to both the reference and the patient group.

The general exclusion criteria for the two groups were as follows: age >70 or <18 years; taking antipsychotic or anti-epileptic medication at any time, and psychotropic drugs that could interfere with attention performance; reduced kidney or hepatic function; past head trauma and loss of consciousness; current alcohol/substance use disorder; pre-existing neurologic or psychiatric disorders; non-corrected hearing or visual impairments; and previous cognitive impairment.

3.2. Mean comparisons: control vs. COVID-19 (Fig. 2)

After adjusting for age, sex, and educational level the MANCOVA showed a significant effect of COVID-19 on attentional performance assessed on the day of discharge from the hospital ($F = 4.520$, $df = 4/52$,

Table 1
Demographic data.

		COVID	Control	Reference	All
		(n = 30)	(n = 30)	(n = 211)	(n = 271)
Female gender, number (%)		14 (47%)	17 (57%)	102 (48%)	133 (49%)
Age (years)	Mean (SD)	47,4 (12,1)	42,8 (11,2)	38,2 (12,1)	39,7 (12,3)
	Minimum	18	22	20	18
	Maximum	61	66	70	70
Length of stay (days)	Mean (SD)	9,5 (12,3)	–	–	–
	Minimum	2	–	–	–
	Maximum	31	–	–	–
Education level	0–8 years (%)	10	0	20	30
	9–12 years (%)	67	0	44	111
	13 or more (%)	23	100	33	156
Visual Attention Test	RT, mean (SD)	458 (72)	375 (38)	343 (47)	359 (61)
	RT, range (median)	329-581 (453)	305-456 (368)	269-519 (328)	269-581 (341)
	VRT, mean (SD)	118 (46)	66 (18)	56 (26)	64 (34)
	VRT, range (median)	52-199 (118)	40-110 (63)	22-149 (51)	22-199 (55)
	OE, mean (SD)	4,7 (7,2)	0,8 (1,6)	0,4 (1,4)	0,9 (3,0)
	OE, range (median)	0-31 (3)	0-6 (0)	0-13 (0)	0-31 (0)
	CE, mean (SD)	2,9 (1,9)	2,6 (2,7)	2,8 (2,2)	2,8 (2,2)
	CE, range (median)	0-7 (3)	0-10 (2)	0-11 (2)	0-11 (2)

RT = reaction time (milliseconds); VRT = variability of reaction time (milliseconds); OE = omission errors; CE = commission errors; SD = standard deviation. - = not applicable. Hospital workers (control group): Physicians (n = 13), Nurses (n = 8), Physiotherapists (n = 1), laboratory employees (n = 6), Psychologists (n = 2).

p = .003, η2 = 0.258). The univariate tests showed that COVID-19 affected omission errors (F = 7.918, df = 1/55, p = .007, η2 = 0.126), RT (F = 14.674, df = df = 1/55, p = .001, η2 = 0.211), and VRT (F = 11.173, df = df = 1/55, p = .001, η2 = 0.169). By contrast, the number of commission errors was not affected by COVID-19 (F = 0.076, df = 1/55, p = .784, η2 = 0.001).

When VRT and RT were replaced by CV, the effect of COVID-19 on attention performance remained significant (F = 3.535, df = 3/53, p = .021, η2 = 0.167), indicating that the VRT effect is not solely driven by RT. The univariate tests confirmed that COVID-19 affected omission errors (F = 7.918, df = 1/55, p = .007, η2 = 0.126) and CV (F = 6.061, df = 1/55, p = .017, η2 = 0.099). As expected, the number of commission errors was not affected by COVID-19 (F = 0.076, df = 1/55, p = .784, η2 = 0.001).

3.3. Standardized scores (Fig. 3)

The inspection of the standardized scores (mean ± standard error of the mean) based on the control group, indicated that VRT was the most affected variable (−3.20 ± 0.49), followed by RT (−2.39 ± 0.36), and CV (−1.74 ± 0.24). These scores were below the cutoff value (−1.5 SD).

Percentiles (controls and patients) based on the reference group (Fig. 4).

Based on the frequency distribution of the 211 subjects of the reference group, we determined the cut points for the 5th percentile for each variable of the CVAT. For VRT, we found 50% of patients (15/30) and 0 controls in the impaired range. For RT, 17 patients (57%) and 1 control (3%) were below the 5th percentile of the reference group. For omission errors, 37% (n = 11/30) of the COVID-19 vs. 10% (n = 3/30) of the control group had a score ≤5th percentile. Conversely, no difference was found for commission errors (3% COVID-19 vs. 10% controls). The percentage of patients with one or more CVAT variables below the 5th percentile of the reference group was 73% (n = 22). By contrast, only 5 controls (16.6%) were impaired in one or more CVAT variables. This difference reached significance ($\chi^2 = 20.75$, df = 1, P < .001).

4. Discussion

The present study showed the presence of specific attentional impairments in COVID-19 patients who had recuperated their physical capabilities on the day of discharge from the hospital. Most of the previous studies were conducted several weeks after discharge (Almeria et al., 2020; Zhou et al., 2020; Mcloughlin et al., 2020; Woo et al., 2020). For instance, a study in Germany with 18 young patients 20–105 days after recovery from mild to moderate COVID-19 showed that 14 (78%)

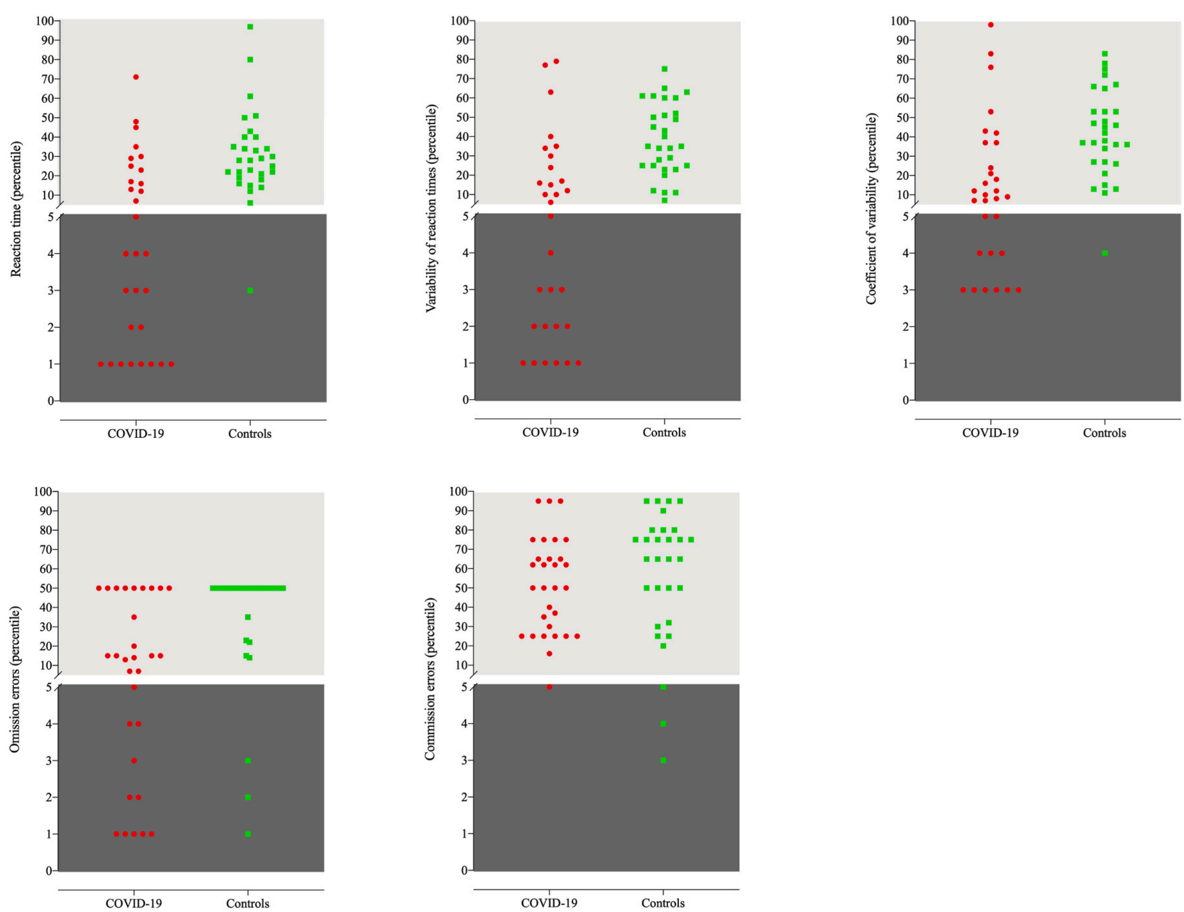

Fig. 4. Distribution of COVID-19 inpatients at discharge (red points) and Controls (green points) according to percentiles of each CVAT variable (on the left side of the plots). The percentiles are based on the frequency distribution of the CVAT's performance by 211 healthy participants who passed in a standardized mandatory exam required for a valid driving license. Thus, the percentiles represent the distributions of the CVAT variables of drivers without any cognitive or health impairment (reference group). Note that the steps increase with 1 for the scale going from 0 to 5. For the scale going from 10 to 100, we start with 10 in steps of 10. The diagonal line represents the 5th percentile. There is some space between this diagonal line and the 10th percentile where the participants who fall within the 5th −10th can be found. Subjects with a performance less than or equal to the 5th percentile of the reference group were considered unsafe drivers. Note that the number of patients below percentile 5 (darkest area of the plots) is higher than the number of controls for all the variables of the CVAT, except for commission errors. After discharge, most post-COVID-19 patients (73%) are potentially at risk because they may be unsafe drivers and cyclists or distracted pedestrians. CVAT= Continuous Visual Attention Test.

patients had sustained mild cognitive deficits as compared to 10 age-matched healthy controls (Woo et al., 2020). Similar results were found in other studies using heterogeneous samples tested several weeks after discharge (Almeria et al., 2020; Zhou et al., 2020; Mcloughlin et al., 2020). Recently, neuropsychological assessments conducted in 57 COVID-19 patients recovering from prolonged hospitalization indicated that attention and executive functions were frequently impaired (Jaywant et al., 2021). Here, we showed that a short attention task detected relevant cognitive deficits in physically recovered patients with COVID-19. Therefore, our findings support that a routine assessment with such tool at the discharge day could provide useful information on whom to send to post-COVID centers for more comprehensive testing later during recovery.

Three CVAT variables were affected (omission errors, RT, and VRT), and one remained unaffected (commission errors). Sustained attention (VRT) was the subdomain most affected. These results are supported by a previous study using a 15-min Go/No-go test in a patient with a mild form of the disease (Tolentino et al., 2021). Therefore, the present data extended previous findings (Hamphire et al., 2021; Ortelli et al., 2021; Tolentino et al., 2021) and further demonstrated that some attention subdomains are more affected than others.

RT was higher in COVID-19 patients as compared to controls. RT is supposed to be linked to brainstem arousal systems and the reticular system to keep alertness (Benghanem et al., 2020). The greater RT exhibited by COVID-19 patients may therefore reflect a direct effect of SARS-CoV-2 on these brainstem circuits necessary for alertness (Yong, 2021). It should be mentioned that patients with long-COVID suffer from fatigue (Ortelli et al., 2021) and it is likely that enhanced fatigue might also be present at day of discharge. The possible presence of fatigue favors the use of cognitive screenings in a faster way as compared to longer neuropsychological batteries. However, we cannot entirely exclude the possibility that fatigue might also be responsible for the higher RT observed in COVID-19 patients. Future investigation should be performed to verify if RT increases as the test progresses, possibly using longer versions of the CVAT. However, the data on RT must be interpreted in conjunction with VRT.

The significantly increased VRT in COVID-19 patients as compared to controls indicated that patients' performance was less stable during the test. Here, the average RT was also found to be significantly greater in patients than in controls. In this regard, previous studies have reported that an increase in VRT could reflect a general slowing of responses driven by RT (Myerson et al., 2007). Wagenmakers & Brown (Wagenmakers and Brown, 2007) have therefore suggested that correcting VRT by RT, i.e., calculating CV, limits VRTs differences due to different baseline RTs. Thus, adding the CV parameter allowed for the study of VRT independent of RT. Here, we showed a significant difference between controls and patients for CV, indicating that the increase in VRT was not solely related to a general slowing process.

The higher VRT in COVID-19 patients affected the stability of response times as the test progressed and thus might produce lapses in attention. Tamm et al. (2012) proposed that simultaneous deficits in omission errors and VRT reflect lapses in attention after slow RTs. Therefore, the finding of a higher number of omission errors in COVID-19 patients suggested that a primary deficit in sustained attention reached a magnitude that affected the attention focus.

Our results showed that a significant percentage (73%) of patients performed below the 5th percentile of the reference group in at least one attention subdomain (RT, VRT, or omission errors). The reference group included only subjects mentally capable of driving who were assessed before the pandemic. Several studies have proven that adequate levels of visual attentional focus, appropriate sustained attention, and normal visuomotor reaction time are essential cognitive abilities for traffic safety (Hopkins et al., 1999). As the patients' showed impairments in specific attention subdomains that are closely related to road traffic safety, our data suggest that COVID-19 patients after discharge may be at risk for road traffic injuries and deaths. We could not address conscious attention allocation or motivational factors for inadequate risk estimation because we were constrained to more basic attention domains of the CVAT. However, higher-order cognitive abilities depend on the integrity of basic attention subdomains (Brower, 2002; Lezak, 2012). These core attention subdomains are a prerequisite for all higher-order cognitive abilities required to be considered a safe road-user (pedestrians, cyclists, or drivers).

While the present study concentrates on driving, the implications might go beyond, as the magnitude of the attentional deficits described in the COVID-19 patients at discharge will most probably not only affect driving, but also safety at work, academic achievements, job performance, and common daily life activities. Accordingly, Burdick and Millet (2021) have argued that mental health consequences of COVID-19 could have substantial societal impact. Therefore, our data suggest that a routine assessment at discharge with the CVAT could provide useful information for objective selection of participants in post-covid rehabilitation programs.

A limitation of this study was the sample size. However, we found very consistent results using an objective assessment tool. Accordingly, the $\eta 2$ of the ANCOVAs was always greater than 0.14, indicating a large effect size (Cohen, 1988). A strength of this study included the use of a sample of patients without delirium during hospital admission who were not subjected to orotracheal intubation. In this regard, previous neuropsychological studies of longer-term outcomes in subjects who required ventilation have reported cognitive impairments in 78% of patients 1 year after discharge (Hopkins et al., 1999, 2005; Mikkelsen et al., 2012). Additionally, Jaywant et al. (2021) showed attention deficits in COVID-19 patients undergoing acute rehabilitation. Therefore, it is likely that critically ill COVID-19 patients who survived will also exhibit significant attention decrements after discharge. However, the generalizability of our findings is limited by the fact that our sample did not include critically ill patients.

Although controls and patients were tested in the same hospital and had the same age and sex distribution, we could not match for educational level. The educational level of the control group was higher than that of the reference group. The finding of lower performance in controls compared to the reference group represents only very indirect evidence that the differences between controls and patients could not be explained by education. Therefore, we included educational level as a covariate in the analyses.

Symptoms associated with so-called "long COVID" have been a growing concern (Graham et al., 2021). Brain fog is just one of many symptoms associated with COVID "long-hauler" syndrome (Nauen et al., 2021). The present report on the functional importance of attentional impairment in COVID-19 patients suggests that further studies are needed to find potential causes of brain fog and thus create guidance for clinicians. The description of cognitive deficits in hospitalized patients recovering from COVID-19 (Jaywant et al., 2021) in conjunction with our findings suggest the need for neuropsychological evaluations in all survivors. However, it is not clear whether the deficits in attention performance found in the patients of this study will persist for a long time after discharge. Although patients with long-COVID suffer from attention deficits, it is not clear whether these are the same people that showed these deficits at discharge. Therefore, longitudinal data are necessary to address this question.

Previous studies have reported that a VRT increase is associated with aging and white matter (WM) abnormalities (Jackson et al., 2012) and a recent systematic review showed evidence that WM abnormalities are higher in COVID-19 patients than could be expected based on age (Egbert et al., 2020). Whilst this study did not assess white matter and cannot make inferences about such outcomes, further investigations using appropriate neuroimaging techniques could assess associations between CVAT outcomes and WM in COVID-19 patients.

COVID-19 infections are known to have a more severe course in patients with certain characteristics/prior diseases, such as obesity, diabetes, hypertension, depression. Although the present study did not include critically ill COVID-19 patients, all these characteristics are known to contribute to cognitive performance. Therefore, one limitation of this study is the absence of data whether patients and controls differ on these aspects. However, irrespective of the underlying mechanism, the deficits in specific attention subdomains exhibited by most COVID-19 patients on the day of discharge from hospital reached values that might impair a wide range of everyday tasks and put road safety at risk. Given millions of people with COVID-19 in conjunction with the worldwide number of road deaths and injuries, we suggest that attentional screenings should be administered on a large scale during the current pandemic. As the CVAT is freely available, it would be possible to use this instrument to facilitate multinational data sharing.

In conclusion, the present study shows that a simple reaction-time Go/No-Go instrument could be used to detect specific attention deficits in COVID-19 inpatients on the day of discharge. This study suggests an objective way to select whom to provide cognitive rehabilitation outpatient programs. Further investigation should be conducted in mild or asymptomatic cases.

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Authors contributions

ACF conducted clinical interviews, performed data collection in all COVID-19 patients, and revised manuscript writing. EvD and JCT performed data collection in the control group, assisted in data analysis and interpretation of results, and revised manuscript writing. SLS elaborated the study design and conceptualization, collected data in the control and the reference groups, performed the statistical analysis, and wrote the manuscript. All authors read and approved the manuscript. ACF is a Ph. D. student under supervision by Prof. SLS.

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