

**Table S2.** What means spousal violence? Definitions provided to study participants.

**Table S3.** Items and response choices of the CoViDoVi Questionnaire and frequency of each response obtained in the survey.

**Table S4.** Limitations of the study.

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## Early attention impairment in a patient with COVID-19

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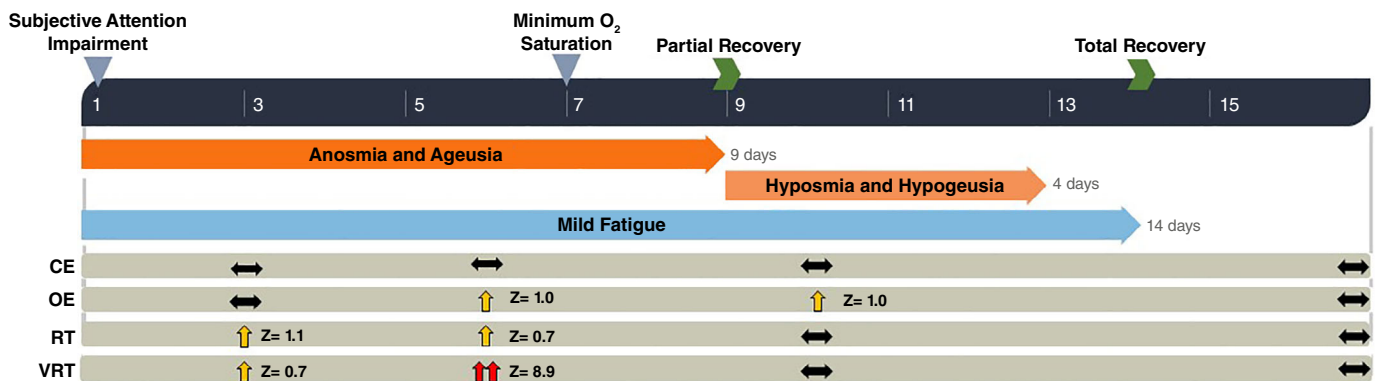
The angiotensin-converting enzyme (ACE2) serves as the main entry into cells for SARS-CoV-2.<sup>1</sup> ACE2 receptors are found in the central nervous system and angiotensin II is an active product of the renin-angiotensin system (RAS).<sup>2</sup> Previous studies have implicated the brain RAS in cognitive functions.<sup>3</sup> Recently, neurologic events and delirium have been described in COVID-19.<sup>4,5</sup> However, no previous research has investigated attention performance. A signed informed consent was obtained from the patient authorizing publication.

A 47-year-old physician suddenly noticed a persistent difficulty maintaining attention while driving. After 2 h, he developed fever, ageusia, and anosmia. On admission, the patient was awake, alert, and oriented to person, place, date, and situation (AAOX4). He denied psychiatric illness, fatigue, excessive workload, or exposure to any recent traumatic event, such as recent death of a patient, friend, or family member. The Mini-Mental State score was 30,<sup>6</sup> body temperature 36.6°C, blood pressure 122/68 mmHg, pulse 72 b.p.m., respiratory rate 16 breaths/min, and oxygen saturation 99% (ambient air). Lung auscultation and laboratory tests were unremarkable (Supplementary Appendix). The antigen test for influenza A and B was negative. A high-resolution computed tomography of the chest was normal (Supplementary Appendix). Nasopharyngeal and throat swab specimens on reverse transcription-polymerase chain reaction analysis tested positive for SARS-CoV-2.

During the disease, the patient remained AAOX4 and without symptoms of depression or anxiety. Although the Mini-Mental State scores always reached the maximum value, he continued to report ‘difficulties to stay focused’ from Day 1 to Day 10 of the illness. On Days 3, 6, 10, and 16, attentional performance was objectively assessed with the Continuous Visual Attention Test (CVAT; Fig. 1), a go/no-go task (Supplementary Appendix) that evaluates attention and its subdomains.<sup>7,8</sup> Impaired performance is explained by slow reaction times (alertness subdomain); high variability of reaction times, indicating lapses in attention as the test progresses (sustained-attention subdomain); omission errors (focused-attention subdomain); and commission errors (response-inhibition subdomain). The test lasts 15 min, and normative values are available.<sup>6–8</sup>

On Day 3, the CVAT performance corroborated the patient’s subjective attention complaints. He exhibited a moderate attentional impairment in two out of the four attention subdomains as compared to the normative values (males, 45–50 years old).

On Day 6, the patient reported a subjective worsening in his concentration, and the second CVAT was performed. Although his physical examination remained normal, the CVAT performance was worse than the Day-3 result. He was impaired in three out of the four attention subdomains. As to the sustained-attention subdomain, he performed above the 95th percentile as compared to age- and-sex matched normative data (a higher percentile indicates a worse performance). Thus, his attentional performance was severely impaired. Eight hours after the worsening of his attentional performance, there was a change in the respiratory status when the patient’s oxygen saturation dropped to as low as 94% while breathing ambient air. This illness progression is consistent with previous reports on signs of worsening of respiratory symptoms in the second week after disease onset.



**Fig. 1** Timeline showing general symptoms and impaired attention functioning. The Continuous Visual Attention Test (CVAT) was used to assess objective attention performance on Days 3, 6, 10, and 16. For each variable of the CVAT, the population mean for the same age and sex of the patient (male, 45 to 50 years old) is set to zero (percentile 50%). The use of a standardized unit (Z-scores) allows direct comparisons across the different variables. Performance between the 75th and 25th percentiles is considered normal (horizontal arrows). Moderate impairment is defined by performance between the 75th and 95th percentiles (vertical yellow arrows). A value higher than the 95th percentile is considered a severe impairment (double vertical red arrow). On Day 1 of illness, the patient reported a subjective attention impairment. On Day 3, the patient performed worse than the 75th percentile in two subdomains (variability of reaction times [VRT] and reaction times [RT]), indicating a moderate attention impairment. On Day 6, the patient performed worse than the 75th percentile in all variables of the CVAT except commission errors (CE), indicating a severe impairment. VRT is

After Day 9, he evolved with clinical improvement. On Day 10, the third CVAT indicated a mild deficit in only one attention subdomain. The response-inhibition subdomain was always spared, since the patient did not have a clinically significant number of commission errors on any of the test occasions. Moreover, he did not present disorientation, psychomotor and autonomic overactivity, hallucinations, difficulty holding a coherent conversation, somnolence, or decreased arousal. In addition, his mental status examination was always unremarkable. Taken together, we suggest that this patient suffered from a more limited dysfunction involving the attentional system.

On Day 16, he did not report any other symptom, and the CVAT was normal. Then, he was submitted to higher-level testing using standardized instruments (described in the Supplementary Appendix). Depression and anxiety were measured using the 7-item Generalized Anxiety Disorder Scale (GAD-7)<sup>9</sup> and the Patient Health Questionnaire-9 (PHQ-9),<sup>10</sup> respectively. The patient's scores did not meet criteria for anxiety (GAD-7 = 3) or depression (PHQ-9 = 6). Cognitive performance (Supplementary Appendix) was always above the 75th percentile (memory, visuospatial perception, and executive functions). He was not taking any psychotropic medication.

The key aspect of this case was the decision made by the patient to seek medical help after the attention impairment. A possible SARS-CoV-2 infection allowed for prompt isolation. An early attention complaint was the first clinical manifestation. A worsening in attention performance on Day 6 preceded the maximum drop in the patient's oxygen saturation. Attentional deficits may be the first sign and the prodromal stage of respiratory impairments in COVID-19.

#### Disclosure statement

The authors have no conflicts of interest to declare.

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#### Supporting information

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

#### Appendix S1. Supporting Information.

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## Effects of contact with COVID-19 patients on the mental health of workers in a psychiatric hospital

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COVID-19 has negatively impacted the mental health of people in general,<sup>1, 2</sup> particularly that of workers treating COVID-19 on the front lines.<sup>3, 4</sup> At our psychiatric hospital, COVID-19 was diagnosed in five inpatients and three workers, and each patient with a confirmed COVID-19 diagnosis was transferred to the designated medical institution for COVID-19, but the ward where other patients had had close contact with COVID-19 patients remained as the COVID-19 ward. Workers in close contact with COVID-19 patients were directed to stay at home, while staff from other wards took over their duties in the COVID-19 ward. With this situation, there was concern that the workers would experience mental health problems related to the nosocomial infection.

Several studies have shown that frontline health-care workers treating patients were at increased risk of anxiety and depression symptoms.<sup>3–5</sup> However, to the best of our knowledge, there is no research on the effects of nosocomial COVID-19 infections in a psychiatric hospital on the mental health of workers, and therefore, we aimed to investigate workers' mental health state after dealing with nosocomial COVID-19 infections in our psychiatric hospital.

Anonymous questionnaires were distributed to all 468 hospital workers composed of doctors, nurses, occupational therapists, psychologists, laboratory technicians, psychiatric social workers, pharmacists, dietitians, and others (e.g., officers), and of these, 426 responded for this study. The characteristics of the participants are shown in Table S1. The questionnaire included items about the workers' sex, age, presence of close contact with COVID-19 patients, presence of housemates, and hospital instructions (staying at home, no change in work, transfer to the COVID-19 ward, or transfer to non-COVID-19 wards). Anxiety and depression were assessed using the Japanese version of the Generalized Anxiety Disorder-7 (GAD-7) and the Japanese version of the Patient Health Questionnaire-9 (PHQ-9).<sup>6, 7</sup> The Mann–Whitney *U*-test and Kruskal–Wallis test were applied to compare the severity of each symptom. To determine the potential risk factors, a multiple-linear regression analysis was performed. Two-way analysis of variance was applied to determine the interaction between the presence of housemates and close contact. This study was approved by the Ethics Committee of Shichiyama Hospital.

The levels of both anxiety and depression were significantly higher in workers who had been in close contact with COVID-19 patients and who had been instructed to stay at home than in those who had not ( $P = 0.013$  and  $P = 0.00006$ , respectively; Fig. S1). Anxiety and depression levels significantly interacted with the presence of housemates ( $P = 0.042$  and  $P = 0.031$ , respectively; Fig. S2). A multiple regression analysis indicated that being female and staying at home (with close contact) increased the degree of both anxiety and depression (GAD-7: sex,  $P = 0.022$ ; stay at home,  $P = 0.010$ ; PHQ-9: sex,  $P = 0.010$ ; stay at home,  $P < 0.001$ ), while the presence of housemates increased anxiety levels only ( $P = 0.035$ ; Tables 1–2; also shown in Fig. S2a). Workers without close contact with COVID-19 patients were divided into three groups: no

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