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)[9] and the Patient Health Questionnaire-9 (PHQ-9),[10] 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.

References

1. Millet JK, Whittaker GR. Physiological and molecular triggers for SARS-CoV membrane fusion and entry into host cells. *Virology* 2018; **517**: 3–8.
2. Xia H, Lazartigues E. Angiotensin-converting enzyme 2 in the brain: Properties and future directions. *J. Neurochem.* 2008; **107**: 1482–1494.
3. Jackson L, Eldahshan W, Fagan S, Ergul A. Within the brain: The renin angiotensin system. *Int. J. Mol. Sci.* 2018; **19**: 876.
4. Helms J, Kremer S, Merdji H *et al*. Neurologic features in severe SARS-CoV-2 infection. *N. Engl. J. Med.* 2020; **382**: 2268–2270.
5. Beach SR, Praschan NC, Hogan C *et al*. Delirium in COVID-19: A case series and exploration of potential mechanisms for central nervous system involvement. *Gen. Hosp. Psychiatry* 2020; **65**: 47–53.
6. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *J. Psychiatr. Res.* 1975; **12**: 189–198.
7. Schmidt G, Alvarenga R, Manhães A, Schmidt S. Attentional performance may help to identify duloxetine responders in chronic pain fibromyalgia patients. *Eur. J. Pain* 2017; **21**: 977–986.
8. Simões EN, Padilla CS, Bezerra MS, Schmidt SL. Analysis of attention subdomains in obstructive sleep apnea patients. *Front. Psych.* 2018; **9**: 435.
9. Spitzer RL, Kroenke K, Williams JB, Löwe B. A brief measure for assessing generalized anxiety disorder: The GAD-7. *Arch. Intern. Med.* 2006; **166**: 1092–1097.
10. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: Validity of a brief depression severity measure. *J. Gen. Intern. Med.* 2001; **16**: 606–613.

Supporting information

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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,[1, 2] particularly that of workers treating COVID-19 on the front lines.[3, 4] 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.[3–5] 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).[6, 7] 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

Table 1. Influence of different factors on Generalized Anxiety Disorder-7 score

Model	Standardized coefficients		Unstandardized coefficients		
	B	Standard error	Beta	*T*	*P*
(Constant)	1.236	1.344		0.919	0.358
Sex	1.148	0.500	0.110	2.294	0.022*
Age	0.365	0.203	0.088	1.796	0.073
Hospital instruction					
No change (reference)	—	—	—	—	—
Stay at home (with close contact)	1.552	0.602	0.133	2.579	0.010*
Transfer to the COVID-19 ward	−0.277	0.741	−0.019	−0.373	0.709
Transfer to other wards	0.458	1.013	0.022	0.453	0.651
Housemate	1.419	0.670	0.101	2.118	0.035*

Predictors for Generalized Anxiety Disorder-7 scores of staff by multiple-linear regression: $^{*}P < 0.05$.

Table 2. Influence of different factors on Patient Health Qestionnaire-9 score

Model	Unstandardized coefficients		Standardized coefficients		
	B	Standard error	Beta	*T*	*P*
(Constant)	3.971	1.378		2.882	0.004**
Sex	1.328	0.513	0.123	2.588	0.010*
Age	−0.090	0.208	−0.021	−0.430	0.667
Hospital instruction					
No change (reference)	—	—	—	—	—
Stay at home (with close contact)	2.279	0.617	0.189	3.695	<0.001***
Transfer to the COVID-19 ward	−0.028	0.760	−0.002	−0.037	0.971
Transfer to other wards	1.430	1.038	0.067	1.378	0.169
Housemate	0.379	0.687	0.026	0.551	0.582

Predictors for Patient Health Qestionnaire-9 scores of staff by multiple-linear regression: $^{*}P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$.

change in work, transfer to the COVID-19 ward, and transfer to other wards. These instructions did not affect workers' anxiety or depression levels ($P > 0.05$, respectively; Fig. S3).

The finding that the presence of housemates increased workers' anxiety and depression might be due to them being afraid of passing COVID-19 to their family members during staying at home and being worried about stigma and social ostracism against their family.[8, 9] We also found that being a female was an independent risk factor for both anxiety and depression, which is consistent with previous research.[3, 5] These results suggest that, in a psychiatric hospital, mental health care is needed, particularly for female workers who are in close contact with COVID-19 patients and who live with housemates.

Contrary to our expectation that workers in a psychiatric hospital tend to be nervous due to the lack of knowledge of coping with infectious diseases,[10] being transferred to the COVID-19 ward did not affect either their level of anxiety or depression. This might be because the inpatients with COVID-19 infection were transferred to other designated medical institutions within 2 days.

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Disclosure statement

The authors declare no conflict of interest.

References

1. Moccia L, Janiri D, Pepe M *et al*. Affective temperament, attachment style, and the psychological impact of the COVID-19 outbreak: An early report on the Italian general population. *Brain Behav. Immun.* 2020; **87**: 75–79.
2. Ahmed MZ, Ahmed O, Aibao Z, Hanbin S, Siyu L, Ahmad A. Epidemic of COVID-19 in China and associated psychological problems. *Asian J. Psychiatr.* 2020; **51**: 102092.
3. Lai J, Ma S, Wang Y *et al*. Factors associated with mental health outcomes among health care workers exposed to coronavirus disease 2019. *JAMA Netw. Open* 2020; **3**: e203976.
4. Zhang W, Wang K, Yin L *et al*. Mental health and psychosocial problems of medical health workers during the COVID-19 epidemic in China. *Psychother. Psychosom.* 2020; **89**: 242–250.
5. Zandifar A, Badrfam R, Mohammadian M *et al*. COVID-19 and medical staff's mental health in educational hospitals in Alborz Province, Iran. *Psychiatry Clin. Neurosci.* 2020; **74**: 499–501.
6. Spitzer RL, Kroenke K, Williams JB *et al*. A brief measure for assessing generalized anxiety disorder: The GAD-7. *Arch. Intern. Med.* 2006; **166**: 1092–1097.
7. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: Validity of a brief depression severity measure. *J. Gen. Intern. Med.* 2001; **16**: 606–613.
8. Bagcchi S. Stigma during the COVID-19 pandemic. *JAMA Netw. Open* 2020; **3**: e203976.
9. Duy CD, Nong VM, Van AN *et al*. COVID-19-related stigma and its association with mental health of health-care workers after quarantine in Vietnam. *Psychiatry Clin. Neurosci.* 2020; **74**: 566–568.
10. Yang M, Wang H, Li Z *et al*. Prevention and control of COVID-19 infection in a Chinese mental health center. *Front. Med.* 2020; **7**: 356.

Supporting information

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

Figure S1 Anxiety and depression in workers having close contact with COVID-19 patients. The (a) Generalized Anxiety Disorder-7 (GAD-7) score and the (b) Patient Health Qestionnaire-9 (PHQ-9) score were significantly higher in the close-contact group (n = 110) than in the non-contact group (n = 316) (P = 0.013 and P = 0.00006, respectively). Statistical analyses were performed using the Mann–Whitney U-test. Bars represent mean ± SEM.

Figure S2 Interaction between the presence of housemates and close contact with COVID-19 patients. There was significant interaction between the presence of housemates and close contact with COVID-19 patients for the (a) Generalized Anxiety Disorder-7 (GAD-7) score and the (b) Patient Health Qestionnaire-9 (PHQ-9) score (P = 0.042 and P = 0.031, respectively). Statistical analyses were performed using two-way analysis of variance (ANOVA). Bars represent mean ± SEM. Housemate (−), close contact (−), n = 53. Housemate (−), close contact (+), n = 15. Housemate (+), close contact (−), n = 255. Housemate (+), close contact (+), n = 103.

Figure S3 Anxiety and depression scores of workers after the directed transfer. There was no significant difference in the (a) Generalized Anxiety Disorder-7 (GAD-7) score or the (b) Patient Health Qestionnaire-9 (PHQ-9) score among the three groups: no change, transfer to the COVID-19 ward, and transfer to other wards (P > 0.05, respectively). Statistical analyses were performed using Kruskal–Wallis test. Bars represent mean ± SEM. No change in work (n = 230), transfer to the COVID-19 ward (n = 58), transfer to non-COVID-19 wards (n = 28).

Table S1 Demographic characteristics of the study sample (n = 426).

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Dopaminergic circuitry in late-life depression and Lewy body disease

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We read with great interest the article by Moriya *et al.*,[1] titled "Low dopamine transporter binding in the nucleus accumbens in geriatric patients with severe depression." Dopaminergic neurons in the ventral tegmental area (VTA) mainly project to the nucleus accumbens (NAc), which plays a critical role in the regulation of mood and motivation. With the development of high-resolution positron emission tomography images acquired with a highly selective radiotracer for dopamine transporter (DAT), the mesolimbic dopaminergic pathway has been recently investigated in patients with major depressive disorder (MDD). Moriya *et al.*[1] demonstrated a mesolimbic dopaminergic abnormality in geriatric patients with MDD using a radioligand of [^{18}F]FE-PE2I. In this study, patients with MDD (mean age, 70.1 ± 6.4 years) showed significantly lower DAT binding potentials in the NAc than the controls, and a trend of lower binding potentials in the putamen was observed. No significant differences in DAT binding potentials were found in the caudate and substantia nigra (SN). In two recent studies using DAT imaging with a radioligand of [^{11}C]PE2I, young or middle-aged patients with MDD showed a significantly lower DAT availability in the putamen and VTA than the controls.[2,3] However, no significant difference was found in DAT availability in the NAc between them. These radiological findings highlighted the involvement of mesolimbic dopaminergic alterations in the development of MDD; however, the role of the NAc in the pathophysiology of geriatric depression could be different from that in young or middle-aged patients with MDD. In the study by Moriya *et al.*,[1] one of 11 MDD patients showed clearly low DAT binding in the putamen and SN; therefore, the authors discussed the existence of a subgroup of MDD patients as having a prodromal phase of Parkinson's disease (PD). In terms of disturbances in monoaminergic transmission from the brainstem nuclei, the potential association with age-related neurodegeneration in late-life depression has been presumed as one of the predisposing factors; however, neuropathological alterations in the context of late-life depression remain unestablished.

Nigrostriatal dopaminergic neurodegeneration associated with Lewy bodies (LB) is the cardinal neuropathological feature of PD and dementia with Lewy bodies (DLB), which results in the development of motor symptoms.[4] The dopaminergic neurons in the VTA were reported to be relatively resistant to pathogenesis of PD,[5] but those in the brains of patients with DLB were poorly understood. Patterson *et al.* investigated neurodegenerative pathology in dopaminergic circuitry in eight PD, 14 PD dementia, and 17 DLB patients in relation to depressive symptoms.[6] Depressed cases showed a significantly greater α-synuclein burden in the SN, VTA, and NAc than the non-depressed cases across the clinical phenotype of LB disorders. Although there was no difference in the neuronal density of VTA between PD and controls, the neuronal density was significantly smaller in DLB than controls. There was no association between depression and Alzheimer-type pathology within nigrostriatal and mesolimbic dopaminergic pathways in the brains of patients with LB disorders. Although depression is commonly observed, even in the prodromal stages of LB disorders,[7,8] there are few pathological data regarding the mesolimbic dopaminergic pathway in relation to late-life depression. Based on a community-based longitudinal study, Wilson *et al.* clinicopathologically investigated the association between the brainstem aminergic nuclei and late-life depressive symptoms in 124 non-demented individuals (mean age at death, 87.7 years).[9] A higher level of depressive symptoms was associated with a higher density of brainstem LB, but not with brainstem neurofibrillary tangles. A higher level of depressive symptoms was associated with a lower density of tyrosine hydroxylase–immunoreactive neurons in the VTA (P < 0.001) and SN (P < 0.03), but not in the locus coeruleus. When the VTA and SN were included in the same model, only the neurons in the VTA were associated with depressive symptoms. No association for tryptophan hydroxylase–immunoreactive neurons in the dorsal raphe nucleus was observed. As a lower neuronal density of VTA was associated with a higher density of brainstem LB, the authors suggested that the association of brainstem LB with depressive symptoms was in part owing to the neuronal density of VTA. Considering that clinicopathological findings suggest a 30–40% threshold of neuronal loss in the SN before the appearance of motor symptoms,[4] early involvement of the mesolimbic dopaminergic system may be associated with prodromal depressive symptoms before fulfilling the clinical criteria for LB disorders.[10] In relation to dopaminergic neurodegeneration, LB-related pathology rather than Alzheimer-type pathology could be a more vulnerable pathological basis for the development of late-life depression. Further neuropathological and radiological studies are needed owing to the limited data regarding mesolimbic dopaminergic pathway in the context of late-life depression.