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LETTER TO THE EDITOR

No changes in cerebral cortical and subcortical structures before and after SARS-CoV-2 infection: Case reports of a patient with schizophrenia and a patient with major depressive disorder

Autopsies of patients who die of severe COVID-19 have shown cerebral infarction, cerebral hemorrhage, and the effects of hypoxia on the brain.[1] Nevertheless, the effects of mild COVID-19 on brain structure are not well understood. A UK Biobank study[2] reported statistically significant differences in left orbitofrontal cortex thinning and increased right lateral ventricle volume before and after SARS-CoV-2 infection in the general population (scan interval was 3.2 ± 1.6 years [mean ± standard deviation]); however, there are no reports in patients with psychiatric disorders. Brain structural abnormalities have been noted in patients with schizophrenia[3–6] and major depressive disorder,[7,8] suggesting that these patients have vulnerable brain structures, and we hypothesize that the effect of COVID-19 on brain structure is even more significant among patients with these psychiatric disorders. In other words, we considered the possibility that the brain structural changes before and after infection with SARS-CoV-2 in patients with those psychiatric disorders could be so pronounced that even a single case, if not a large number of cases, could be detected. This study examined brain structural changes before and after SARS-CoV-2 infection in patients with schizophrenia and major depressive disorder.

Case 1: A woman developed schizophrenia at the age of 19 years. She underwent T1-weighted magnetic resonance (T1) imaging at the age of 21 years, after which she contracted COVID-19. The patient required hospitalization due to COVID-19. At the age of 22 years, she underwent T1 imaging again. The scan interval of T1 before and after SARS-CoV-2 infection was 13 months. The Positive and Negative Syndrome Scale (PANSS) scores at the time of imaging were almost the same before and after infection (PANSS Positive: 18 and 19 points before and after infection, respectively; PANSS Negative: 22 and 17 points before and after infection; PANSS General: 40 and 32 points before and after infection).

Case 2: A woman developed major depressive disorder at the age of 32 years. At the age of 36 years, she underwent T1 imaging. She then contracted COVID-19 4 months after imaging. She recovered at home. T1 imaging was performed again 3 weeks after infection. The scan interval of T1 before and after SARS-CoV-2 infection was 4.5 months. The Hamilton Depression Rating Scale 17 (HDRS-17) score was 14 at the time of T1 imaging before infection and 4 at the time of T1 imaging after infection. Three months after pre-infection T1 imaging and 1 month before SARS-CoV-2 infection, the HDRS-17 score was 8, which means the depressive symptoms had already improved before COVID-19 infection.

The cortical thicknesses and surface areas of 68 cortical regions of interest and the volumes of 16 subcortical regions were calculated from the T1 imaging data by using FreeSurfer.[9] Data from 100 healthy control subjects were used to correct the data from these patients for longitudinal natural changes in healthy control subjects. All participants in this study provided written informed consent based on the approval of the institutional review board of the National Center of Neurology and Psychiatry, and privacy protection was taken into consideration.

In Case 1, no thinning of the left orbitofrontal cortex or increased volume of the right lateral ventricle were observed after infection. Neither of these were observed in Case 2. Furthermore, there was no area showing significant changes in the investigated brain structures after COVID-19 infection in either case (Supporting Information: Table S1).

This is the first report to examine changes in brain structure in patients with psychiatric disorders before and after SARS-CoV-2 infection. In the two cases we examined here, psychiatric symptoms did not worsen even after COVID-19 infection. In the patient with mood disorder (Case 2), depressive symptoms had even improved. These suggested that post-COVID-19 conditions had less of an effect on psychiatric symptoms compared with treatment effects or natural changes. In parallel with psychiatric symptoms, the brain structures we studied were similar before and after COVID-19 infection, even regarding left orbitofrontal cortex thinning and right lateral ventricle volume, which were shown to change in a previous study,[2] suggesting that there were fewer post-COVID-19 condition effects. However, the changes in psychiatric symptoms and brain structures

associated with COVID-19 infection might depend on individual patients. Future studies with larger populations should be designed to clarify the effects of COVID-19 infection on psychiatric symptoms and brain structure in patients with schizophrenia or major depressive disorder.

AUTHOR CONTRIBUTIONS

Junya Matsumoto contributed to conceptualization, investigation, data curation, formal analysis, writing original draft, and writing review and editing. Satsuki Ito contributed to formal analysis, validation, resources, investigation, data curation, and writing review and editing. Ryuichi Yamazaki contributed to formal analysis, validation, and writing review & editing. Kiyotaka Nemoto contributed to methodology, formal analysis, data curation, and writing review and editing. Masaki Fukunaga contributed to resources, investigation, methodology, data curation, and writing review and editing. Fumitoshi Kodaka contributed to formal analysis, software, and writing review and editing. Harumasa Takano contributed to resources, data curation, and writing review and editing. Naomi Hasegawa contributed to investigation and writing review and editing. Kenichiro Miura contributed to formal analysis, validation, resources, investigation, methodology, data curation, and writing review and editing. Ryota Hashimoto contributed to conceptualization, methodology, investigation, resources, data curation, writing review and editing, supervision, project administration, and funding acquisition.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

Raw data supporting this study cannot be shared because the consent to disclose raw data from the participants was not obtained.

ETHICS APPROVAL STATEMENT

This study was approved by the institutional review board of the National Center of Neurology and Psychiatry (approval number: A2019-036).

PATIENT CONSENT STATEMENT

All participants in this study provided written informed consent.

CLINICAL TRIAL REGISTRATION

N/A

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.