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Dynamic changes in near-infrared spectroscopy (NIRS) findings in first-episode schizophrenia: a case report

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Abstract
The clinical course of schizophrenia is characterized by recurrence and chronicity and has a large burden on society. Nevertheless, diagnosis of schizophrenia is based only on distinctive symptoms and the disease course. Near-infrared spectroscopy (NIRS) is a useful method for measuring changes in the hemoglobin concentration in the cortical surface area and reflects brain function. We measured NIRS four times during the clinical course in a patient with first-episode schizophrenia.

A 17-year-old woman admitted to our hospital because of hallucinations, delusions and appetite loss. After treatment with low-dose antipsychotics, NIRS findings showed a prompt increase in the cerebral blood volume in the frontal region. On the basis of the clinical course of this patient, we introduce a new point of view, namely, that NIRS findings may be useful as a state marker that indicates the severity of schizophrenia in some cases.

Key words: near-infrared spectroscopy, schizophrenia, homovanillic acid, biomarker, state marker

Introduction
Schizophrenia is a major psychiatric disease that generally includes delusions and auditory hallucinations. The clinical course of schizophrenia is characterized by recurrence and chronicity and has a large burden on society. Thus, early diagnosis and intervention are very important. Nevertheless, due to insufficient biological data, diagnosis is based only on distinctive symptoms and the disease course. Near-infrared spectroscopy (NIRS) is a useful tool for measuring changes in the hemoglobin concentration in the cortical surface area and reflects brain function1. Recent studies have shown that frontal hemodynamic patterns measured by NIRS can be a biomarker for the diagnosis of schizophrenia2. However, some researchers have stated that findings detected with NIRS may not be trait markers but state markers3,4. Therefore, in the present case, we measured NIRS a total of four times during the clinical course of the acute phase of a patient with first-episode schizophrenia. We used the verbal fluency task because it is easily performed successfully by most subjects with psychiatric disorders and it produces distinct differences in findings among some diagnostic groups of psychiatric disorders2. Additionally, we measured plasma levels of homovanillic acid (pHVA), a major metabolite of dopamine, using high-performance liquid chromatography.

Case presentation
The patient was a 17-year-old female who had...
been seriously abused during her childhood. After her parents divorced, she became socially withdrawn over 1 year. After that, she was admitted to our hospital in May 2015 because she ate hardly anything. Careful examination after admission revealed that she suffered from auditory and olfactory hallucinations and showed abnormal behaviors based on these symptoms. As a result, her social function was significantly below the level achieved prior to the onset. Because these disturbances lasted for at

Fig. 1A. Waveforms of oxygenated hemoglobin during cognitive activation during the word fluency task.

Fig. 1B. Grand average waveforms of oxygenated hemoglobin in the frontal region (CH 25-28, CH 36-38, and CH 46-49). In this image, the vertical axis shows [oxy-Hb] concentration (mMmm) and the horizontal axis the time (s).
least 1 year, we diagnosed her with first-episode schizophrenia. Administration of low-dose antipsychotics resulted in rapid and dramatic improvement in her hallucinations and delusions. Her motivation and social cognition also seemed to have improved, and thus, she began to try forming relationships with other patients. Her Global Assessment of Functioning (GAF) score increased from 25 to 80. GAF subjectively rates social, occupational, and psychological functioning. Simultaneously, her pHVA level decreased (31.3 ng/ml → 20.6 ng/ml). On day 129, 73 days after leaving the hospital, her pHVA further decreased (15.5 ng/ml).

In addition, we measured NIRS three times during her hospitalization and one time after she left the hospital. NIRS findings showed a lower oxygenated hemoglobin ([oxy-Hb]) increase during the first half of the task compared to the second half and an [oxy-Hb] re-increase in the post-task period, which is a characteristic pattern of schizophrenia (Fig. 1A). Particularly, the cerebral blood volume in the frontal region improved during her clinical course (Fig. 1B), and the integral value level was greatly elevated on day 129.

**Materials and methods**

In the present case, NIRS during the word fluency task was measured during the clinical course of first-episode schizophrenia. In brief, oxygenated hemoglobin ([oxy-Hb]) and deoxygenated hemoglobin ([deoxy-Hb]) were measured with a 52-channel (CH) NIRS machine (Hitachi ETG-4000; Hitachi Medical Corporation, Tokyo, Japan) at two wavelengths of near-infrared light (695 and 830 nm), the absorption of which was measured, and [oxy-Hb] and [deoxy-Hb] were calculated. The distance between pairs of source-detector probes was set at 3.0 cm, and each measured area between pairs of source detector probes was defined as a “channel (CH)”. The probes of the NIRS machine were fixed with 3 × 11 thermoplastic shells, with the lowest probes located along the Fp1-Fp2 line according to the international 10-20 system used in electroencephalography.

**Discussion**

We experienced a patient with the first episode of schizophrenia in whom NIRS could be measured longitudinally. Low-dose antipsychotics led to a prompt increase in the cerebral blood volume in the frontal region as shown by NIRS and a decrease in the pHVA level concomitant with the improvement in clinical symptoms. The patient showed prompt improvement in symptoms after medication, however, [oxy-Hb] increased after a while. Although this reason has not been clarified, similar phenomenon has been reported in the SPECT study of depression. On the other hand, since pHVA decreased stepwise, it could not be said that there was a correlation between pHVA and [oxy-Hb]. Furthermore, it seemed that [oxy-Hb] decreased on day 53, but in fact, there was no change at the integral value level (Fig. 1C). Thus, it is suggested that temporal gap between the improvement of symptoms and the increase in NIRS findings can exist.

One study has examined the relationships between the HVA level and the pathophysiology of schizophrenia, and in some cases, the pHVA level may be useful as a state marker. To the best of our knowledge, in this report, we examined for the first time sequential changes in NIRS findings during the process of improvement in a patient with acute schizophrenia. Therefore, we suggest that NIRS findings may be useful as a state marker that indicates the severity of schizophrenia in some cases. Sequential NIRS changes must be investigated in

![Fig. 1C. The integral values of [oxy-Hb] in the frontal region measured by NIRS. In this image, the vertical axis shows the integral value and the horizontal axis the time course (day).](image-url)
additional cases of schizophrenia to confirm this hypothesis.

Conflict of interest

All authors declare that they have no biomedical financial interests or potential conflicts of interest.

References