I N JAPAN, NEAR-INFRARED spectroscopy (NIRS; optical topography) was recently approved for health insurance as an auxiliary laboratory test for the differential diagnosis of the depressive state of bipolar disorder (BD) and schizophrenia from that of major depression. In this test, the time course of the changes of hemoglobin levels in the forehead during a verbal fluency task is used as a supplementary method for differential diagnosis. This approval was based on the result of a multicenter collaborative study. However, there was also a criticism that it was premature to approve this test based on limited scientific evidence. Most of the patients examined in the initial study were medicated, and it is not known whether the observed findings were affected by medication. The principle of NIRS is based on modified Beer–Lambert law and the hemoglobin level is measured in the unit of mM-mm, the product of concentration and optical path length, which hampers the comparison across subjects. In addition, it was also reported that contamination of signals outside the brain can confound the obtained data. It is not known whether the use of this laboratory test promoted correct diagnosis of BD in clinical settings.

According to our experience, only one of eight patients who visited Rokubancho Mental Clinic to ask for a second opinion after being diagnosed as having BD by NIRS in other clinical facilities was diagnosed as having BD (Table S1). The other seven patients were diagnosed as having major depressive disorder or another condition. We compared the data with other patients who had visited this clinic after being diagnosed as having BD without the use of NIRS in other clinical facilities (File S1). The rate of concordant diagnosis in patients diagnosed as having BD according to NIRS (1/8, 12.5%) was significantly lower than that in controls (30/44, 68.1%, $P = 0.005$).

This observation should be interpreted with caution, because patients who doubt the given diagnosis may tend to visit other clinics for a second opinion. Thus, we also examined the data among the patients who participated in genome research at RIKEN. Among 51 subjects who volunteered during a similar period, seven replied that they had been diagnosed as having BD according to NIRS. The rate of concordant diagnosis was significantly lower in the patients diagnosed as having BD according to NIRS (3/7, 42.8%) than in other patients (38/44, 86.3%, $P = 0.021$). These findings indicated that patients who are not diagnosed as having BD I or BD II by a clinical interview are diagnosed as having BD when NIRS is used. It cannot be totally ruled out that those patients who were diagnosed as having BD according to NIRS would indeed develop genuine (hypo) manic episodes, sometime in the later course of their illness. Such a possibility, however, should actually be tested in a prospective study.

Recently, the Japanese Society of Mood Disorders (JSMD) published a statement to caution the diagnosis of BD according to NIRS alone. The statement says that it is not appropriate to put more value on NIRS than clinical assessment and the diagnosis should be based on DSM-5 or ICD-10, even when NIRS is performed. Our experiences reported here endorse the validity of the statement by the JSMD.

This study was approved by the Wako Third Research Ethics Committee of RIKEN.

DISCLOSURE STATEMENT

There is no conflict of interest.

REFERENCES

1. Fukuda M. Optical topography as an auxiliary laboratory test for differential diagnosis of depressive state: Clinical application of near-infrared spectroscopy (NIRS) as the first trial for approved laboratory tests in psychiatry. Seishin Shinkeigaku Zasshi 2015; 117: 79–93.
2. Takizawa R, Fukuda M, Kawasaki S et al. Joint Project for Psychiatric Application of Near-Infrared Spectroscopy (JPSV-NIRS) Group Neuroimaging-aided differential diagnosis of the depressive state. Neuroimage 2014; 85: 498–507.
3. Cyranoski D. Neuroscience: Thought experiment. Nature 2011; 469: 148–149.
4. Takahashi T, Takikawa Y, Kawagoe R, Shibuya S, Iwano T, Kitazawa S. Influence of skin blood flow on near-infrared spectroscopy signals measured on the forehead during a verbal fluency task. Neuroimage 2011; 57: 991–1002.
5. Kataoka M, Matoba N, Sawada T et al. Exome sequencing for bipolar disorder points to roles of de novo loss-of-function and protein-altering mutations. Mol. Psychiatry 2016; 21: 885–893.
6. Japanese Society of Mood Disorders. A statement on the significance of optical topography test in the diagnosis of bipolar disorder and depression. [Cited 16 August 2017.] Available from URL: http://www.secretariat.ne.jp/jsmd/ (in Japanese).

SUPPORTING INFORMATION

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

Table S1. Number of patients diagnosed as having bipolar disorder among subjects who visited Rokubancho Mental Clinic or participated in genome research at RIKEN

File S1. Supporting methods.

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