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Clinical Applications of Functional Near-Infrared Spectroscopy in Children and Adolescents with Psychiatric Disorders

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The purpose of this review is to examine the clinical use of functional near-infrared spectroscopy (fNIRS) in children and adolescents with psychiatric disorders. Many studies have been conducted using objective evaluation tools for psychiatric evaluation, such as predicting psychiatric symptoms and treatment responses. Compared to other tools, fNIRS has the advantage of being a noninvasive, inexpensive, and portable method and can be used with patients in the awake state. This study mainly focused on its use in patients with attention-deficit/hyperactivity disorder and autism spectrum disorder. We hope that research involving fNIRS will be actively conducted in various diseases in the future.

Key Words: Near-infrared; Biomarkers; Mental disorders; Child; Adolescent.

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INTRODUCTION

The diagnosis of psychiatric disorders is based on descriptive symptoms and signs. Patients who cannot accurately identify and express their symptoms or refuse to express their symptoms may be difficult to diagnose. This is also the case for children who have difficulty recognizing and verbalizing their thoughts at the stage of development or for adolescents who are forced to meet psychiatrists by their parents. To compensate for this, several attempts have been made to objectively evaluate the therapeutic prognosis of children and adolescents with psychiatric disorders. Endogenous substances or various neuroimaging techniques, such as quantitative electroencephalography (QEEG) [1,2], event-related potentials [3,4], positron emission tomography (PET) [5,6], single-photon emission computed tomography (SPECT) [6], and functional magnetic resonance imaging (fMRI) [5,7,8], have been used to diagnose psychiatric disorders. However, most children with attention-deficit/hyperactivity disorder (ADHD) have hyperactivity symptoms are difficult to assess due to poor cooperation in neuroimaging evaluation or frequent movements, resulting in many artifacts. In particular, techniques such as MRI require staying motionless for an accurate evaluation.

Functional near-infrared spectroscopy (fNIRS) is a type of spectroscopy that uses a light source between and 650−1000 nm that can pass through organic tissues. fNIRS is relatively easy to use for evaluating children with ADHD because it takes a short time to complete. It is possible to measure the cortical oxygenation levels with hemoglobin using a noninvasive, inexpensive, and portable method [9]. It is used as an adjunct diagnostic tool for various psychiatric disorders because it can be used to evaluate brain activity (cognitive function or emotional change) using tasks such as the verbal fluency task [10]. Additionally, it can be used to evaluate children and adolescents, as it can be easily worn and does not involve exposure to radiation.

In this review, we will examine the clinical use of fNIRS in children and adolescents with psychiatric disorders.

ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER

Few studies have used fNIRS in psychiatric disorders in children and adolescents, although ADHD is the most studied disorder [11-13]. Studies using fNIRS have focused on the differ-

ence in hemodynamic activity according to the symptoms of ADHD or the prediction of treatment response to medications through various cognitive tasks. First, the examination of the differences in hemodynamic activity according to symptoms is based on the following principle: the core symptoms of ADHD (inattention, hyperactivity, and impulsivity) are related to executive function impairment and mainly reflect the function of the prefrontal cortex (PFC) [14-16]. Among the executive functions, impaired inhibition is frequently observed in children with ADHD in fNIRS studies using the stroop task, reverse stroop task (RST), or Go/No-Go task [11-13,17]. Negoro et al. [13] reported that children with ADHD (ADHD group) showed significantly smaller changes in oxy-hemoglobin than typically developing children (TDC group) in the inferior lateral PFC bilaterally during the Stroop color-word task. Yasumura et al. [11,12] reported that inattention severity in the ADHD group was negatively correlated with right lateral PFC activity during the RST. In another study by Yasumura et al. [18], children with ADHD had lower activity in the right PFC than the TDC, and the left PFC showed a compensatory function. However, no age-related changes in the right PFC were observed in children and adolescents with ADHD. Kaga et al. [17] reported that children with ADHD showed a greater decrease in hemodynamic activity in the right PFC than those in the TDC group using fNIRS during the Go/No-Go task. Although the studies differed slightly in each study in terms of method, statistics, or results, the hemodynamic activity of the right PFC in the ADHD group was consistently lower than that in the TDC group.

Second, the studies that predicted the treatment responsiveness of ADHD treatment were as follows: In a study by Monden et al. [19], during the Go/No-Go task, the ADHD group reported reduced hemodynamic activity in the right inferior frontal gyrus (IFG) and middle frontal gyrus (MFG) than the TDC. In addition, the hemodynamic activity of the right IFG and MFG was normalized 1.5 h after methylphenidate administration, and no such change was observed after placebo administration. Consistent with findings from other studies [19-21], fNIRS has been identified as an effective tool for predicting the therapeutic response of methylphenidate and atomoxetine. In addition, after administration of MPH and atomoxetine, the hemodynamic activity of the right PFC was increased, and the right hemisphere was lateralized. Meanwhile, in the study by Nakanishi et al. [22], there was no statistically significant change in hemodynamic changes after MPH administration. Studies by Nakanishi et al. [22] and Sanefuji et al. [23] found contradictory results from other studies [19-21,24], such as left-lateralized effect after pharmacotherapy. The results may differ depending on the research and statistical method; therefore, future research is needed to confirm consistent results.

AUTISM SPECTRUM DISORDER

As fNIRS is advantageous for indicating the functional activation of the brain of an awake child and infant, there have been ongoing studies on autism spectrum disorder (ASD). Many studies have focused on the differences in brain activity in children with ASD, and some studies have focused on functional connectivity between brain regions [25,26]. These results suggest that fNIRS can be used as a biomarker for the early diagnosis of ASD. It may be more helpful for children younger than 3 years or infants in the high-risk group for whom clinical diagnosis is difficult.

Research focusing on brain functional activation can be divided into studies related to social and non-social difficulties. First, looking at studies focusing on social difficulties, Lloyd-Fox et al. [27,28] found that high-risk infants aged 4–6 months showed decreased activation in the temporal cortex in response to visual and auditory social stimuli compared to low-risk controls. Braukmann et al. [29] also reported weaker activation in the right posterior temporal cortex in high-risk infants. Kita et al. [30] reported that children with ASD had a decreased response in the IFG compared to the TDC during self-face recognition. In addition, Mori et al. [31] showed that children with ASD had low IFG activation when imitating facial expressions. Zhu et al. [32] found that children with autism and Asperger syndrome showed abnormal activity in the frontal cortex, such as in the IFG and PFC, when performing joint attention tasks. Studies examining non-social difficulties focused on differences in brain activity when tasks related to language, working memory, and inhibition control were performed. Studies on language tasks have yielded inconsistent results. Minagawa-Kawai et al. [33] reported weaker functional lateralization in the temporal cortex and Wernicke's area in patients with ASD than in the TDC in relation to awareness of sound and language processing. Gallagher et al. [34] reported clear laterality during a language task in children with pervasive developmental disorders. Kuwabara et al. [35] reported that the ASD group showed decreased prefrontal activation compared to the TDC during the letter fluency task, and Iwanami et al. [36] reported the same result in Asperger patients. Similar results were found in studies on working memory tasks [37,38]. Funabiki et al. [39] and Xiao et al. [40] found reduced activation of the right PFC in patients with ASD during the listening and ignoring task and Go/No-Go task, which evaluated inhibitory control ability.

Regarding brain functional connectivity, Keehn et al. [41] reported that the functional connectivity between the frontal and temporal cortex decreased in high risk infants with sib-

lings with ASD compared to in the low risk infants. Li and Yu [42] observed a decrease in inter-region connectivity in the right PFC in patients with ASD compared with in the TDC. Furthermore, Li et al. [43] showed decreased functional connectivity between the bilateral temporal lobes in children with ASD.

Another important aspect of the clinical application of fNIRS in ASD is the possibility of neurofeedback training as a clinical intervention. One study found improved facial recognition in the group receiving real-time feedback in high-functioning children with ASD [44]. Studies have also reported that patients with ASD show improvement in working memory and performance in the presence of anxiety and mood disorders when receiving neurofeedback [45]. Research on the effect of neurofeedback on patients with ASD is still limited, but future studies are expected to increase the clinical applicability because of the advantages of fNIRS-neurofeedback, such as practicability and low cost [46].

MOOD DISORDER AND OTHER DISORDERS

Research on the use of fNIRS in children and adolescents with mood disorders is limited. Relatively, there are many studies related to depression in adults, and previous studies consistently reported that adults with depression showed reduced oxy-hemoglobin activity in the PFC during cognitive tasks compared to healthy controls [47,48]. Previous MRI studies [49-51] reported reduced left prefrontal activation in many areas of the PFC in patients with major depressive disorder. In a study by Lee et al. [52] on the use of fNIRS, reduced hemodynamic changes were observed in the left PFC in the major depressive disorder group than in the healthy control group. This study confirmed that the oxy-hemoglobin changes in the left ventrolateral PFC mediated the indirect effect of depression severity on the severity of suicidal ideation [52]. Thus, the possibility of fNIRS as a useful auxiliary tool was confirmed even when evaluating suicidal ideation. Mood disorders and suicidal ideation in children and adolescents require further research.

Nagamitsu et al. [53] found a significant difference between children with anorexia nervosa (AN) and the TDC group in relation to the result of the Eating Attitudes Test (EAT-26) result and changes in oxyhemoglobin using fNIRS. The AN group showed higher EAT-26 scores and higher oxyhemoglobin than the TDC group during the task, but the TDC group showed higher EAT-26 scores and lower oxyhemoglobin during the task. The difference in prefrontal hemodynamic responses between the AN and TDC groups was shown using fNIRS. In addition, fNIRS has been used to predict the risk of psychopathology in young children [54], predict the postoperative status of pediatric cardiac transplantation patients [55], and confirm expressive and receptive language brain lateralization in the presurgical assessment of epileptic children [56].

CONCLUSION

In this study, we reviewed the clinical application of fNIRS in children and adolescents with psychiatric disorders. Many studies involving QEEG, event-related potentials, PET, SPECT, and fMRI have been conducted to identify biomarkers or objective markers. Compared to other tools, fNIRS has the advantage of being a noninvasive, inexpensive, and portable method with the ability to evaluate patients in the awake state. We expect that research involving fNIRS in various diseases will be actively conducted in psychiatric research and clinical settings.

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Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

Author Contributions

Conceptualization: Yeon Jung Lee, Ji-Sun Kim. Data curation: Yeon Jung Lee, Yun Sung Lee, Jeong Eun Shin. Funding acquisition: Yeon Jung Lee. Investigation: Yeon Jung Lee, Minjae Kim, Ji-Sun Kim. Methodology: Yeon Jung Lee, Minjae Kim, Ji-Sun Kim. Project administration: Yeon Jung Lee, Minjae Kim, Ji-Sun Kim. Resources: Yeon Jung Lee, Yun Sung Lee, Jeong Eun Shin. Supervision: Yeon Jung Lee, Ji-Sun Kim. Validation: all authors. Writing—original draft: Yeon Jung Lee, Minjae Kim, Ji-Sun Kim. Writing—review & editing: all authors.

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