Application of NIRS as a non-invasive and supportive tool for Autism spectrum disorders

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Abstract: We have previously proved prefrontal hemodynamic change in autism spectrum disorder (ASD) subjects according to switching task using near infrared spectroscopy (NIRS) lacks synchronizing evoke of oxygenated hemoglobin, although the task performance rates were almost equivalent to the controls. Therefore, next we have applied the neurofeedback (NFB) system using NIRS for ASD subjects to establish their task-related PFC activity control. The NFB system using wireless NIRS was preliminarily applied to 4 ASD individuals with a session consists of 7 consecutive trials. They partially showed improvement in PFC blood oxygenation response to the self-stimulation of neurofeedback by plotting oxy-Hb and d(oxy-Hb)dt and detect barycentric points appearance. Additionally, the average data of working memory and non-working memory switching task, stroop test, anxiety test, self-evaluation test, and mood test, were all improved during the NFB training, as well as follow-up check. These results suggests us that it might be possible to apply NIRS as a non-invasive sub diagnostic tool as well as active supporting tool for ASD subjects.

Keywords: autism spectrum disorder, biofeedback, anxiety

1. Introduction
Autism spectrum disorder (ASD) is a congenital neurological disorder characterized by impairment of socialization, abnormalities in communication, limited activity, and curiosity. Defects in the prefrontal cortex (PFC) and its signal processing have attracted interest in understanding this complex impairment of brain function in ASD, and numerous studies, including recent ones using functional neuroimaging, have been reported. However, clear and consistent interpretation has not been well established until date.

Recently we have examined prefrontal hemodynamic change according to reciprocal disposition of working memory and non-working memory tasks using NIRS to compare high-functioning ASD subjects with controls. An evoked cerebral blood oxygenation change was instantly observed in response to the task switch in the controls but not in ASD subjects, although the task performance rates were almost equivalent.

We therefore hypothesized that the delayed prefrontal activation in response to the outer stimulation would be improved if ASD subjects are actively trained by a neurofeedback (NFB) system using NIRS.

2. Subjects and Methods
Four ASD subjects were participated in the study. Subject T; male, age 17, Full Scale IQ was 86, Verbal IQ was 91, and Performance IQ was 83 by the Wechsler Intelligence Scale for Children-III (WISC-III). Subject I; male, age 27, Full Scale IQ was 73, Verbal IQ was 92, and Performance IQ was 54 by the Wechsler Adult Intelligence Scale-III. Subject S; male, age 19, Full Scale IQ was 96, Verbal IQ was 110, and Performance IQ was 80 by the WISC-III. Subject U; male, age 17, Full Scale IQ was 87, Verbal IQ was 80, and Performance IQ was 97 by the WISC-III.

All subjects had been diagnosed by pediatric neurology and psychology specialists on the basis of developmental history and current presentation, according to the Diagnostic and Statistical Manual of Mental Disorders V and the Japanese version of the Autism Diagnostic Interview-Revised. The study was approved by the Research and Ethical Committee of Bunkyo University, and written informed consent was obtained from each subject or their legal guardian prior to the study.

Neurofeedback using NIRS-based BCI system was established and applied to this study. Two-channeled handy NIRS (PocketNIRS, Dynasense, Hamamatsu, Japan) was connected with PC via wireless system, and the sensors were placed symmetrically on the forehead of the subjects so that the bottom margin of the 2 optodes was identical to the T3—Fp1-Fpz-Fp2-T4 line of the international EEG 10/20 system.

Subjects were accommodated in a comfortable chair, staring at a monitor in front of them. During the task period, they were ordered to change the color of the monitor into red, which reflects increase of oxy-Hb in their left prefrontal cortex, because the feedback was set in the left side probe. One task lasts 30s, accompanied by encompassing rest time of 15s with closing eyes and relaxing. One trial consists of 6 tasks, and 7 trials, which was performed average twice a week, was considered as one session. On the first and the last trial of each session, working memory and non-working memory switching task, stroop test, anxiety test, self-evaluation test, and mood test were performed to evaluate the NFB training. Also follow-up evaluation was done within 1 to 3 months after the session with anxiety test, self-evaluation test, and mood test.

During performance of the NFB training and switching task, concentration changes in oxy-Hb, deoxygenated (deoxy-) Hb, and total Hb were continuously measured with a time resolution of 0.229 second. Collected data was analyzed by plotting barycentric points of PFC activation induced by each task and rest stimulus, on the coordinate axis of oxy-Hb and deoxy-Hbdt. Further analysis was done by calculating weighted separability (WS), using an original calculation developed by Tsunashima, et. al., roughly shown as below:

Degree of (1)
separability |
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Weighed separation (WS) = (Number of resting barycentric points) x Degree of (1)
separability / Number of switching barycentric points

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3. Results

Figure 1 shows an example of oxy-Hb and deoxy-Hb concentration change during NFB training of Subject T. This individual participated in 2 sessions of training. Figure 1A shows the result of the first trial of the first session. Evoked oxy-Hb concentration was dominantly observed in rest period, while the oxy-Hb concentration tended to drop during the task period. Figure 1B shows the result of the last trial of the second session. After 14 trials during 9 months of period, the subject’s oxy-Hb in the PFC showed the tendency of increase during the task, and decrease during the rest, however still apart from the perfectly-trained status as reported previously\(^\text{12}\).

For further analysis, we plotted the center point of each trial’s oxy-Hb barycentric points along with \(d(\text{oxy-Hb})/dt\) of the Subject T as shown in Figure 2. Figure 2A shows the result of the first trial of the first session. The barycentric points of the task period are scattered in the third quadrant, whereas the barycentric points of the rest period are mainly appeared in the first quadrant. These results were contradictory to what was expected from the experimental instruction. On the other hand, as shown in Figure 2B, after 14 trials of 2 sessions, Subject T showed altered barycentric points distribution, such that barycentric points of the task period and rest period are both appeared in the first and the fourth quadrants.

Calculated WS of the first trial of the first session was 0.515, and was increased to 25.8 on the third trial of the first session. However, it again dropped to as low as 0.217 in the first trial of the second session, and finally it ended up with WS of 0.110 in the last trial of the second session.

The data of working memory and non-working memory switching task, stroop test, anxiety test self-evaluation test, and mood test, were also collected from the participants, and the average of 4 participants were evaluated.

The average task performance rate of working memory task in the first of the session (n=4) was 38.75%, whereas the average task performance rate of working memory task in the last of the session (n=4 ) was 58.75%.

The average latency time of incongruent stimuli of the stroop test was 1065.25 msec in the first of the session (n=4), and in the last of the session (n=4) was reduced to 1030.25 msec. The average latency time of congruent stimuli of the stroop test was 844.25 msec in the first of the session (n=4), and in the last of the session (n=4) was reduced to 837.75 msec.

With the STAI anxiety questionnaire, the average score of trait anxiety (n=4) was 48.50 in the first session, 45.00 in the last session, and 32.50 in the follow-up check. The average score of state anxiety (n=4) was 39.75 in the first session, 30.50 in the last session, and 29.00 in the follow-up check.

Total mood disturbance (TMD) score, which represents disorder of the total mood status including anxiety, anger, depression, confusion, and vigor was calculated from the POMS mood questionnaire. The average TMD score (n=4)
was 21.50 in the first session, 10.25 in the last session, and 0.50 in the follow-up check.

The self-check sheet was applied to the participants to check objective overview of themselves in terms of the ASD characteristics. The average score was (n=4) 18.50 in the first session, 21.75 in the last session, and 21.25 in the follow-up check.

4. Discussion

NFB is a relatively newly developed biofeedback12, and the training system with EEG has obtained certain popularity in the United States as a substitution for a conventional treatment with medication to the subjects with anxiety, depression, epilepsy, and ADHD patients13-16. Although the effects of NFB are still controversial, this method is not as invasive as medication, and is considered as one of the optimums to the child with these disorders to apply. It is reported that many of the children with ADHD who were treated using EEG has long-term effect in sleep state improvement, which particularly is important for the neurodevelopmental disorders to improve their daytime symptoms17.

Usage of NIRS for NFB system as a detecting tool is relatively necessary to realize this preliminary study. Establishing a sub-diagnostic tool using working EEG., and is more ideal to the children and attention deficit psychological status and the self-cognition test was all improved that a session consists of 7 trials is insufficient. Still, activation improvement to the task order was seen, it seemed that a session consists of 7 trials is insufficient. Still, improvement in the working memory task performance rate and latency time in stroop test encourage us to consider the possible effectiveness of NIRS-based NFB application to ASDs, who has characteristics social difficulties based on PFC functional disorders. Moreover, the fact that all those psychological status and the self-cognition test was all improved as an average during and after the training showed that the NFB training might be applicable not only for the PFC activation, but also for the anticipation of improving anxiety and depression, that are frequent comorbidity with ASD.

Two-channeled NIRS is advantageous in its handiness to the EEG, and is more ideal to the children and attention deficit subjects. Establishing a sub-diagnostic tool using working memory and non-working memory switching task with NIRS measurement, as well as consecutive NIRS-based NFB training system could be a very conventional, non-invasive, and non-existing ever innovation for ASD. Further investigation is necessary to realize this preliminary study.

Reference