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Original Article

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Effects of Personalized Cognitive Training Using Mental Workload Monitoring on Executive Function in Older Adults With Mild Cognitive Impairment

OPEN ACCESS

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HIGHLIGHTS

- Machine learning based on fNIRS data could be useful in monitoring mental workload.
- Personalized cognitive training would be effective in improving executive function.
- Mental workload monitoring using fNIRS could provide personalized cognitive training.

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Conflict of Interest
The author has no potential conflicts of interest to disclose.

ABSTRACT

Although a variety of cognitive training has been performed, its optimally personalized delivery is still unknown. This study established the mental workload classification model using a convolutional neural network based on functional near-infrared spectroscopy-derived data. The dorsolateral prefrontal cortex (DLPFC) while thirty individuals with mild cognitive impairment (MCI) performed spatial working memory testing was found to be a considerable indicator to classify 3 levels of mental workload with an accuracy of over 86%. In the next step, forty subjects with MCI were randomly allocated into the experimental group (EG) that received cognitive training with mental workload-based difficulty adjustment or the control group (CG) that received conventional cognitive training. To compare both groups, the Trail Making Test Part B (TMT-B) and hemodynamic responses in the DLPFC during the TMT-B were measured. After the 16 training sessions, the EG subjects achieved a greater improvement in the TMT-B than the CG subjects ($p < 0.05$). Also, the EG subject showed a significantly lower DLPFC activity during the TMT-B than the CG subject ($p < 0.05$). In sum, the EG subjects better performed executive function with lower energy from the DLPFC. These findings imply that the importance of mental workload monitoring to provide personalized cognitive training.

Keywords: Cognition; Cognitive Dysfunction; Machine Learning; Prefrontal Cortex

INTRODUCTION

As the importance of early intervention in Alzheimer's disease (AD) has been highlighted, an interest in mild cognitive impairment (MCI), a pre-clinical stage of AD, is getting important [1]. Given the results of studies reporting that 10%–30% of older adults with MCI proceed to AD, the development of an effective intervention for the elderly with MCI is urgent [1]. Individuals with MCI show declines in working memory and executive function heavily depending on the prefrontal cortex (PFC), which is one the of hallmarks of MCI. Therefore, cognitive training designed to target the PFC could be effective for individuals with MCI [2].

On the other hand, to deliver effective cognitive training, it needs to be tailored to subject's cognitive level [3,4]. To date, unfortunately, the difficulty level of cognitive training has been mainly adjusted according to the success rate of the subject's performance in previous studies [4,5]. Specifically, when a subject's performance exceeds an 80% success rate, training proceeds by increasing its difficulty level to the next level [5]. However, this approach has a limitation in that it cannot be objectively tailored in real time. Thus, it is necessary to tailor the training difficulty level based on not only performance but also brain-derived signals which could be objectively assessed such as brain activity [3,4].

Among various brain imaging techniques, functional near-infrared spectroscopy (fNIRS) has gained growing attention to obtain brain-derived data due to its ease of use, high portability, relatively low cost, and high ecological validity, compared to other techniques [6]. Accordingly, attempts have been made to predict tailored difficulty levels of cognitive training based on fNIRS-derived brain activity [3,7,8]. However, while most of prior studies on algorithms based on fNIRS-derived brain activity only predicted the difficulty of a cognitive task through machine learning techniques, they did not use them for tailored training [3,7,8]. In addition, in previous studies implementing customized cognitive training based on brain activity, only changes in brain activity were analyzed during each session, resulting in that no factor considering both cognitive performance and brain activity in targeted brain areas such as neural efficiency was investigated in terms of clinical benefits [7-9].

Therefore, the first goal of this study was to establish the brain activity-derived mental workload monitoring algorithm using machine learning techniques and investigate its accuracy. The second goal of this study was to examine the effects of tailored cognitive training using mental workload monitoring.

MATERIALS AND METHODS

Experiment 1

Subjects

Thirty patients with MCI were recruited from senior welfare centers in Seoul and Asan, South Korea. The inclusion criteria were as follows: 1) a subjective memory complaint, 2) an objective memory impairment confirmed as the Seoul Neuropsychological Screening Battery, 3) intact global cognitive function confirmed as the Korean version of Mini-Mental Status Examination (≥ 24), and 4) intact activities of daily living. The exclusion criteria were as follows: 1) dementia diagnosed by a physician, 2) psychiatric or neurological disorders, and 3) no participating in any therapeutic program for cognitive function. All subjects provided written informed consent before inclusion according to the Declaration of Helsinki (2004). This study was approved by the Institute of Review Board of Soonchunhyang University (202204-SB-056).

Procedures

All subjects performed the computerized Corsi Block Tapping (CBT) Task, and their PFC activity was measured while performing the CBT task. Before the measurement, each subject's forehead was securely covered with a headband, and the fNIRS probes were placed in line with the electroencephalography 10–20 standard system. During the measurement, each subject sat in a chair and was asked to perform the CBT task using a computer on the desk in front of the subject. Each subject was asked to limit superfluous motions other than mouse movement to input his/her responses to reduce artifacts caused by his/her movements. The measurement lasted until the time a subject completed the task.

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Apparatus

The computerized CBT task was used to induce mental workload. In each trial of the CBT task, 9 white squares were randomly placed on a computer monitor. Some of the squares changed their color from white to red in a sequential manner and subjects were instructed to memorize the locations and sequences. Afterward, subjects were to point out the changed squares in a forward manner by clicking a mouse. In this study, the number of squares to be changed ranged from 3 to 5, resulting in 3 difficulty levels of sessions. Each session included 10 trials, and there were 3 sessions in ascending order of difficulty levels (3 → 5).

PFC hemodynamic responses were measured by the fNIRS device (OctaMon; Artinis BV, Elst, The Netherlands) with 8 channels (8 emitters and 2 detectors). All fNIRS data were sampled with a frequency of 10 Hz. Oxygenated hemoglobin (HbO) and deoxygenated hemoglobin (HbR) were detected at 760 and 850 nm of wavelength, respectively. Inter-optode distances were fixed at 3 cm and a total of 8 channels were distributed to target the left and right dorsolateral PFC (DLPFC) [10,11].

Data preprocessing

OxySoft software (version 3.0.52; Artinis BV) was used to analyze the fNIRS data. The fNIRS data were preprocessed by a low band-pass filter to reduce artifacts of cardiac and respiratory responses. The blood concentration changes were computed according to the modified Beer-Lambert Law [11]. HbO signals were only used as they are more sensitive to cognitive reactions than HbR [12,13]. Mean changes in HbO concentration (mHbO) were derived from 8 channels (the right and left PFC), and mHbO using a 3–12 seconds window was analyzed considering that functional neural activity takes more than 10 seconds to reach a significant activation level [11,14].

Convolutional neural network (CNN)

A statistical t-value was obtained to represent the statistical significance of mHbO concerning the baseline, and it was used to generate the *t*-map for a topographic image [15] (**Fig. 1**). The size of each image was set to at least 224 × 224 pixels according to a CNN structure. The images for thirty subjects were classified into 3 classes based on the 3 levels of difficulty of the CBT task, resulting in a total of 120 images.

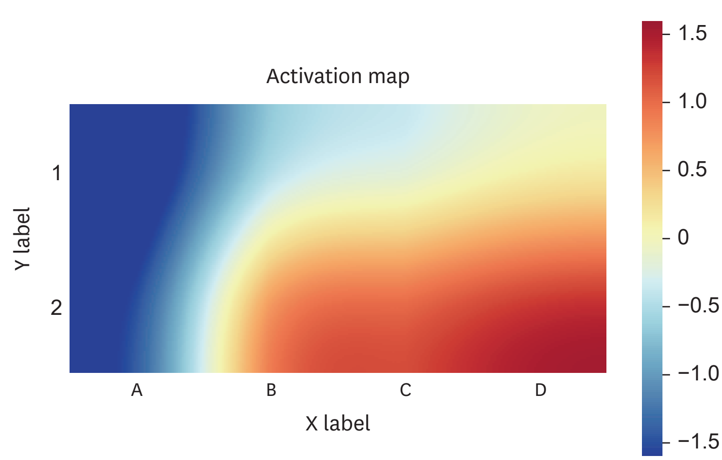

Fig. 1. *t*-map representation in the prefrontal cortex.

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For deep learning, the size of the data set is highly correlated with its performance [16], so the number of data sets was increased using the image augmentation technique in this study. This is a method of acquiring additional deformed images by making the previously acquired images different from the originals by using processing maneuvers such as tilting, inversion, or rotation. This can increase deep learning performance by further extracting and learning salient features [16]. Therefore, 3,000 images for each class were constructed by increasing the original data set using only enlargement and reduction.

To improve the CNN performance, the VGGNet model was used, and Categorical Cross-Entropy was applied to the loss function. To update the weight for the error of the loss function, the Adam optimizer was applied. To verify CNN's capability to classify mental workload, accuracy was investigated.

In this study, considering that the CNN model might have suffered from an overfitting problem because of the small number of data sets, this study employed 5-fold cross-validation to decrease the influence of overfitting on the accuracy. The number of times (epochs) to learn was set to 10 times, and the batch size per batch was set to 8.

Statistical analysis

All data were analyzed using the SPSS for Windows version 22.0 (SPSS Inc., Chicago, IL, USA). To confirm the normality of outcome data, the Kolmogorov-Smirnov test was used. The demographic characteristics of subjects were analyzed using descriptive statistics. To confirm the difference in accuracy and mHbO across the difficulty levels of the CBT task, the Friedman test was used and then a post hoc Wilcoxon signed-rank test was performed to assess the difference between levels. Statistical significance was set at $p < 0.05$.

Experiment 2

Design

This study was a randomized controlled trial, and subjects were randomly allocated into the experimental group (EG) receiving personalized cognitive training using an fNIRS-derived mental workload monitoring algorithm or the control group (CG) performing conventional cognitive training with performance-based mental workload monitoring (**Fig. 2**). The randomization was conducted by a blinded experimenter using computer-generated random numbers. Outcome measures were implemented at pre- and post-intervention by a blinded assessor. The intervention involved 16 sessions performed 2 times a week for 8 weeks.

Subjects

Forty older adults with MCI over 65 years old were recruited from local senior centers in Seoul and Asan, South Korea. The inclusion criteria in accordance with a previous study [10] and were as follows: (a) had subjective memory complaint, (b) had a Korean version of Montreal Cognitive Assessment (MoCA-K) score lower than 23 [17], and (c) had the ability to perform independently basic activities of daily living. Exclusion criteria were as follows: (a) dementia diagnosed by a clinician, (b) neurological or psychiatric disorders, (c) auditory or visual impairment, and (d) participation in cognitive training within the last 3 months.

The sample size was calculated by using G*Power 3.1.7 software (University of Dusseldorf, Dusseldorf, Germany). The effect size was set at 1.41 with power levels at 0.90 and alpha levels at 0.05, resulting in a minimum of 9 subjects [4].

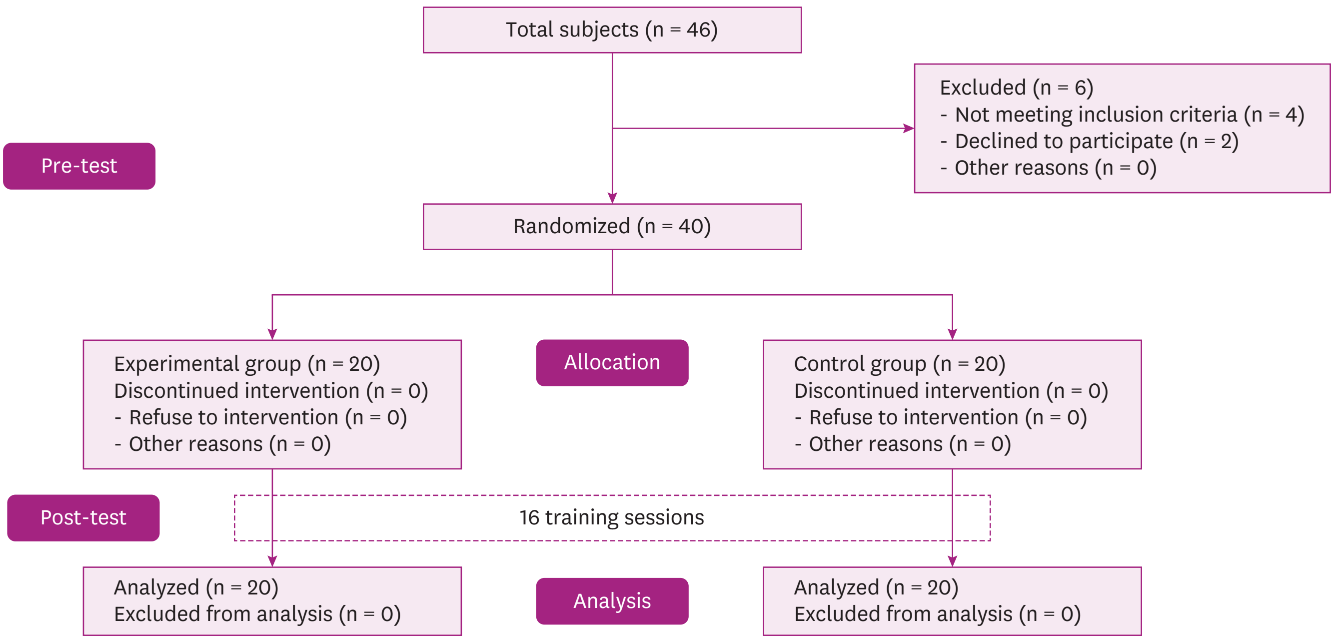

Fig. 2. Flow diagram of subjects in this study.

Intervention

The EG subjects performed the computerized CBT task used in Experiment 1. During each session, the EG subjects were equipped with fNIRS to measure their PFC activity for providing personalized training difficulty levels. According to the CNN model based on the subject's PFC activity, the difficulty levels of the CBT task ranging from a low (circles to be remembered: 3) to a high level (circles to be remembered: 5) was adjusted after 10 trials (approximately 90 seconds) in each session. For example, the CNN model predicted the subject's PFC activity during 10 trials as a middle level (circles to be remembered: 4), resulting in sustaining a current difficulty level next 10 trials.

In contrast to the EG, the CG subjects performed the CBT task without the CNN classification model. Instead, the difficulty levels of the CBT task were adjusted based on how successfully the CG subjects performed on every 10 trials. Specifically, a success rate of 80% or higher increased the difficulty level, while a rate of 50% or lower decreased the difficulty level. Otherwise, the difficulty levels were maintained.

Both groups received cognitive training for 16 sessions (20 minutes a session for 8 weeks). Two occupational therapists with 3 years of clinical experience performed all training sessions and they sufficiently practiced the use of the CNN model using the subject's PFC activity.

Outcomes

The Trail Making Test Part B (TMT-B) was used to assess executive function as a primary outcome that is related to executive function depending on the PFC [18]. The TMT-B is an assessment tool to evaluate attention, working memory, and cognitive flexibility [19]. The TMT-B requires connecting randomly presented numbers and Korean alphabets alternatively as quickly as possible. Randomly listed numbers range from 1 to 13, and randomly listed Korean alphabets were from "Ga" to "Ta." The performance of the TMT-B was represented by the reaction time to complete it, and a lower reaction time means higher executive function [20].

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DLPFC activity during the TMT-B was measured as a secondary outcome using the fNIRS device used in Experiment 1. During the measurement, each subject sat in a comfortable chair and was asked to perform the TMT-B. To minimize artifacts induced by his/her movement, they were instructed to minimize unnecessary movements other than their arm movement to complete the TMT-B. In this study, mHbO concentration in the PFC was averaged. All fNIRS data were sampled with a frequency of 10 Hz with Oxysoft version 3.0.52. All outcomes were performed before and after the intervention by the blinded occupational therapist with 5 years of experience.

Statistical analysis

All data were analyzed using the SPSS for Windows version 22.0 (SPSS Inc.). To confirm the normality of outcome data, the Kolmogorov-Smirnov test was used. The demographic characteristics of both groups were analyzed using the χ^2 test and the independent t-test. After the intervention, differences in outcome measurements intra-group and inter-group were compared using paired t-test and independent t-test. Statistical significance was set at $p < 0.05$.

RESULTS

Experiment 1

General characteristics

Gender, age, education level, and scores of the MoCA-K were investigated. Seventeen (56.7%) of the subjects were female, and the average age was 75.77 years. The average education level was 4.70 years, and the average score of the MoCA-K was 22.90 points (**Table 1**).

Performance on the CBT task and the hemodynamic response

There was a significant difference in accuracy according to the difficulty levels of the CBT task ($p < 0.001$) (**Fig. 3**, **Table 2**). Specifically, as the difficulty level increased, the accuracy decreased. In addition, there was a significant difference in the PFC activity across the difficulty levels of the CBT task. Specifically, as the difficulty level increased, the PFC activity increased ($p < 0.001$) (**Fig. 3**, **Table 2**). In sum, increased mental workload induced a decrease in accuracy and an increase in brain activity.

Table 1. General characteristics of subjects in Experiment 1 (n = 30)

Characteristics	Subjects
Age (yr)	75.77 ± 5.99
Sex	
Male	13 (43.3)
Female	17 (56.7)
Education periods (yr)	4.70 ± 4.64
MoCA-K (scores)	22.90 ± 1.97

Shown are mean value ± standard deviation or number (%).
MoCA-K, Korean version of the Montreal Cognitive Assessment.

Table 2. Accuracy of the Corsi Block Tapping task and brain activity across the difficulty levels

3-block		4-block		5-block	
Accuracy	mHbO (μM/mm)	Accuracy	mHbO (μM/mm)	Accuracy	mHbO (μM/mm)
0.952 ± 0.038	0.921 ± 0.063	0.781 ± 0.050	1.030 ± 0.087	0.488 ± 0.056	1.294 ± 0.185

Shown are mean value ± standard deviation.
mHbO, mean of oxygenated hemoglobin.

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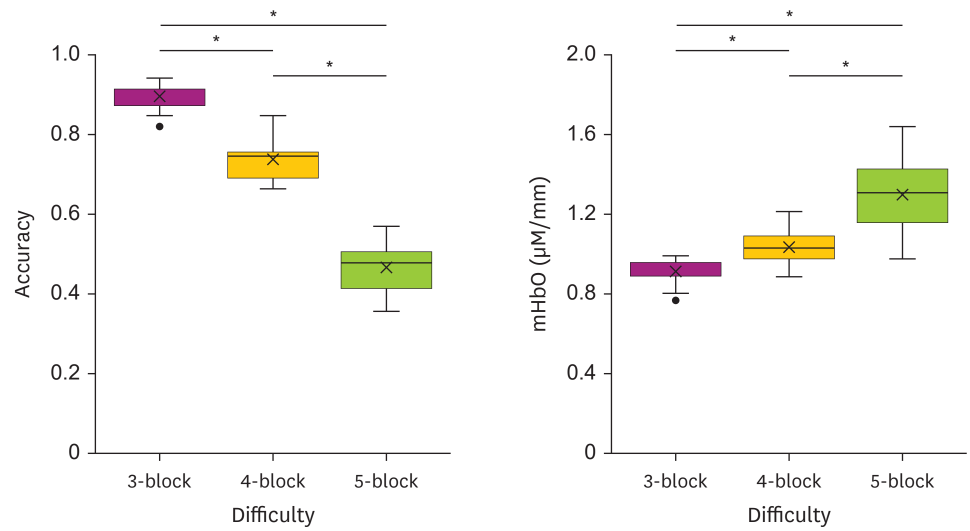

Fig. 3. Accuracy and hemodynamic response across the 3 levels.
mHbO, mean of oxygenated hemoglobin.
*$p < 0.05$, Wilcoxon signed-rank test following the Friedman test.

CNN classification accuracy

The statistical t-value indicated that mHbO from the DLPFC is the most accurate indicator for the difficulty level classification among the PFC sub-regions (**Table 3**). As a result of building the CNN model through 10 times repetition, the accuracy of the VGG-16 algorithm ranged from 0.86 to 0.97.

Experiment 2

General characteristics of participants

There were no significant differences in subjects' characteristics between the EG and CG (all p's > 0.05) (**Table 4**).

Behavioral performance

After the 16 training sessions, both groups showed a faster reaction time in the TMT-B (EG: $p < 0.001$; CG: $p < 0.001$) compared to the baseline (**Table 5**). On the other hand, the EG subjects achieved a significantly greater improvement in the TMT-B than the CG subjects (p <

Table 3. The t-value across the PFC areas

Characteristics	PFC				
	Whole	Lateral	Medial	Dorsolateral	Ventromedial
t-value	3.481	5.432	2.694	8.635	4.697

PFC, prefrontal cortex.

Table 4. General characteristics of subjects in Experiment 2 (n = 40)

Characteristics	Experimental group (n = 20)	Control group (n = 20)	t/χ²
Age (yr)	73.6 ± 3.26	73.4 ± 3.21	0.196
Sex			0.107
Male	7	8	
Female	13	12	
Education periods (yr)	6.00 ± 3.07	6.15 ± 3.70	0.139
MoCA-K (scores)	19.45 ± 1.82	18.80 ± 1.64	1.186

Shown are mean value ± standard deviation.
MoCA-K, Korean version of the Montreal Cognitive Assessment.

Table 5. Comparison of executive function between both groups (n = 40)

TMT-B (sec)	Experimental group (n = 20)	Control group (n = 20)	Between-group differences
Pre-intervention	236.60 ± 22.15	246.50 ± 27.09	6.30 ± 2.69*
Post-intervention	224.95 ± 20.70	241.15 ± 27.29	
Within-group changes	11.65 ± 10.72†	5.35 ± 5.48†	

Values are expressed as median ± standard deviation.
TMT-B, Trail Making Test Part B.
*$p < 0.05$; †$p < 0.001$.

Table 6. Comparison of the dorsolateral prefrontal cortex activity between both groups (n = 40)

mbO (μM/mm)	Experimental group (n = 20)	Control group (n = 20)	Between-group differences
Pre-intervention	0.622 ± 0.141	0.635 ± 0.114	0.059 ± 0.008*
Post-intervention	0.556 ± 0.135	0.628 ± 0.115	
Within-group changes	0.066 ± 0.036‡	0.014 ± 0.022†	

Values are expressed as median ± standard deviation.
mHbO, mean of oxygenated hemoglobin.
*$p < 0.05$; †$p < 0.01$; ‡$p < 0.001$.

0.05) (**Table 5**). This finding suggests that personalized cognitive training was more helpful in improving executive function than conventional cognitive training.

Hemodynamic response

mHbO in the DLPFC during the TMT-B significantly decreased in both groups (EG: $p < 0.001$; CG: $p < 0.01$) compared to the baseline (**Table 6**). When comparing between groups, the EG showed a considerably higher decrease in the DLPFC activity than the CG ($p < 0.001$) (**Table 6**). These results imply that the EG subjects performed executive function with less energy of the DLPFC.

DISCUSSION

This study aimed at establishing an fNIRS-derived mental workload monitoring algorithm using a CNN model and investigating the effects of personalized cognitive training using mental workload monitoring on executive function in older adults with MCI. As a result, the CNN model based on fNIRS data could classify 3 levels of mental workload with over 86% accuracy, and personalized cognitive training induced a significant improvement in executive function and decreased the DLPFC activity compared to conventional cognitive training with performance-based mental workload monitoring.

In Experiment 1, a significant difference in the accuracy of the CBT task across the 3 levels was observed. Also, DLPFC activity was significantly changed across the levels, which means that DLPFC activity responded differently according to the levels. These findings imply that fNIRS-derived data can objectively measure and classify mental workload. On the other hand, out of the PFC sub-regions, the DLPFC was found to be a considerable region to establish the mental workload monitoring algorithm using a CNN model. Neuroimaging studies have consistently reported that the DLPFC plays a crucial role in executive function [21]. Specifically, the DLPFC is closely correlated to working memory, goal-driven attention, task switching, planning, and problem-solving [21]. In this study, since mHbO was measured during the CBT task, one of working memory tasks, the increased DLPFC activity was selectively showed the highest t-value to classify mental workload. Indeed, a previous study indicated that the DLPFC was specifically correlated to working memory compared to other

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parts of the PFC so the DLPFC was targeted as a region of interest [22], supporting that the neural correlate of working memory was selectively confirmed in this study.

In Experiment 2, after the 16 training sessions, the EG subjects achieved higher performance on the TMT-B than the CG subjects. Considering that the TMT-B is widely used to assess executive function, it could be interpreted that personalized cognitive training was more beneficial to improve executive function than conventional cognitive training. Since the TMT-B requires an ability to switch attention and mental flexibility which are some of the sub-elements of executive function [20], improved performance on the TMT-B could be considered as an enhanced executive function. These findings suggest that DLPFC activity could be a better indicator to identify a tailored difficulty level than task performance, resulting in a greater improvement in training's effect.

On the other hand, after the 16 training sessions, DLPFC activity during the TMT-B was significantly decreased in both groups. Notably, DLPFC activity decreased more significantly in the EG subjects than in the CG subjects. This result implies that the EG subjects used less energy from the DLPFC than CG during cognitive testing. Given decreased DLPFC activity coupled with enhanced executive function in the EG subjects, personalized cognitive training could induce an improvement in neural efficiency in the DLPFC, which is consistent with previous findings [4,18,23]. Previous studies indicated that this coupling could be regarded as an improvement in neural efficiency [4,18,23], supporting the interpretation of this finding. Taken together, it is possible to interpret the improvement in executive function as the result of the DLPFC's increased neural efficiency.

Considering that most of the related studies used paper-based neuropsychological assessment to assess the effects of cognitive training, the findings of this study have a clinical implication that objective and quantitative monitoring is essential to provide personalized cognitive training. In terms of clinical usefulness, mental workload monitoring in real-time would be helpful to clinicians interacting with subjects performing cognitive tasks, by notifying the subject's cognitive burden and then instantly adjusting their difficulty levels. In a previous study, a difficulty level of a cognitive task was adjusted using mental workload monitoring for a subject having an excessive mental load, resulting in that executive function being considerably improved [4]. This finding supports the possibility of the use of an fNIRS-derived mental workload monitoring system and fNIRS-based neuro-feedback training in the field of cognitive rehabilitation, and this system would supplement the conventional difficulty adjustment system heavily depending on the subject's cognitive performance [4], supported by a meta-analysis of fNIRS-based neuro-feedback training [24].

In terms of the applicability of fNIRS, there have also been attempts to measure mental workload in healthy subjects using fNIRS. In a previous study, fNIRS was successfully used to measure the mental workload of pilots' brain activity in the frontal lobe while operating a flight simulator [25]. Furthermore, fNIRS-derived data during cognitive testing could be used to discriminate patients with MCI or AD from healthy aging [11,26]. These findings suggest that fNIRS is applicable regardless of the level of cognitive impairment. On the other hand, while fNIRS has been mainly used in cognitive-related studies, it has also been used to investigate muscle endurance or recovery after physical exercise by measuring muscle oxygenation [27] or to report motor function improvements by measuring changes in motor areas in the cerebral cortex [28], implying that fNIRS would be used in a variety of ways.

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Despite the clinical usefulness of the current findings, this study has several limitations. Firstly, due to the lack of channels in the fNIRS device, other brain areas were not investigated. The role of PFC networks with parietal and temporal lobes in executive function needs to be considered [29]. Even though, the PFC plays a critical role in executive function, how PFC networks can more accurately measure mental workload needs to be addressed in future studies. In addition, other machine learning techniques should be further considered to analyze more data derived from multi-channels of fNIRS devices that can cover PFC networks instead of statistical analysis which could not be satisfying to detect MCI [11,30]. Secondly, Although, data augmentation techniques enabled to have a larger sample than the originally acquired sample, there was a lack of original data to establish the optimized mental workload monitoring algorithm. Since the number of data is closely correlated to the accuracy of machine learning models, future studies need to be implemented with a larger sample. Finally, evidence for personalized cognitive training's effects on daily life was not investigated. Given the importance of ecological validity in the field of rehabilitation, not only neural correlates but also the impact of daily life needs to be investigated [31].

In conclusion, this study revealed that personalized cognitive training using the fNIRS-derived mental workload monitoring algorithm could be more beneficial to improve executive function and neural efficiency in the PFC, compared to performance-based cognitive training. This finding shed new light on the usefulness of mental workload monitoring during cognitive training to provide tailored cognitive challenges. In future studies, the clinical usefulness of various fNIRS-derived indicators from whole brain regions in a larger sample needs to be investigated to accurately monitor mental workload during various cognitive challenges.

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