International Journal of Gerontology 16 (2022) 316–321
https://doi.org/10.6890/IJGE.202210_16(4).0001

International Journal of Gerontology

journal homepage: http://www.sgecm.org.tw/ijge/

Review Article

Effects of Functional Near-Infrared Spectroscopy-Based Neuro-Feedback Training on Cognitive Function: Systematic Review and Meta-Analysis

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ARTICLE INFO

Accepted 11 April 2022

Keywords:
functional near-infrared spectroscopy,
neuro-feedback,
meta-analysis,
cognition

SUMMARY

Background: Recently, numerous studies on non-invasive neuro-feedback training for improving cognitive function have been explored to identify its feasibility. However, little is known about the clinical efficacy of functional near-infrared spectroscopy-based neuro-feedback (fNIRS-based NF) training in individuals with or without cognitive impairment.
Method: Studies on fNIRS-based NF training were searched through Embase, Medline, PubMed, Web of Science, PsychINFO, and Google scholar and then four studies were finally selected. The overall cognitive domains, working memory, and executive function were separately pooled to investigate fNIRS-based NF training's effect size.
Results: The overall effect on cognitive outcomes across four studies was large (Hedges'g = 0.682, confidence interval (CI) = 0.079–1.285) without publication bias. Moderate to large effects were found for working memory (Hedges'g = 1.143) and executive function (Hedges'g = 0.406) without publication bias. fNIRS-based NF training was beneficial in improving working memory and executive function.
Conclusion: Therefore, this finding shed new light on fNIRS-based NF training as a promising treatment for improving cognitive function.

1. Introduction

Cognitive training has been widely used for patients with or without cognitive impairment to maintain or enhance cognitive function in a variety of settings.[1] Previous studies have revealed that cognitive training could facilitate neuro-plastic mechanisms in the brain, resulting in improving cognitive function in people with or without cognitive impairment.[2]

Among various cognitive training approaches, neuro-feedback (NF) in real time using the level of brain activity has been adopted.[3] Most prior studies have adopted electroencephalography (EEG) and functional magnetic resonance imaging (fMRI) for providing NF.[4,5] In these studies, NF combined with computerized cognitive training programs was found to be effective in improving cognitive function and facilitating neuro-plasticity in targeted brain areas.[5] Since subjects choose the best strategy to use efficient neural resource for optimal performances by monitoring and regulating themselves with NF, NF has been proven to maximize effectiveness of cognitive training.[5,6]

Recently, functional near-infrared spectroscopy (fNIRS), a growing neuroimaging method, has attracted critical attention for NF because of its practicability in clinical settings. fNIRS with light sources and detectors uses near-infrared light which could be directed onto the surface of the head. fNIRS can measure brain hemodynamics by detecting amount of light absorbed by hemoglobin and thus fNIRS indirectly estimates brain activation in the underlying brain tissue.[7] fNIRS has advantages over other neuroimaging devices. First, it is easier to use, portable, inexpensive and safe than fMRI. Second, fNIRS tolerates more head motion than EEG and fMRI. These advantages make it possible to use fNIRS in more naturalistic settings.[8]

In previous studies, subjects performed a computerized cognitive task with behavioral feedback regarding their performance on the task as well as their oxygenated hemoglobin (HbO_2) in the regions of interest (ROIs).[7,9] Specifically, previous studies have consistently indicated that subjects showed increased the prefrontal cortex (PFC) activity as cognitive load increases. In addition, repetitive cognitive task implementation could result in decreased PFC activity, reflecting improved neural efficiency.[10] Taken together, these findings indicate that fNIRS-based NF training could be also beneficial in improving cognitive function and neural efficiency as well as other fMRI or EEG-based NF training.

However, to date, there has been no optimal protocol of fNIRS-based NF training such as duration, NF stimulus, a number of channel of fNIRS, and statistical significance through comprehensive systematic review and meta-analysis. Moreover, considering existing reviews mainly focus on the applicability of fNIRS-based brain-computer interfacing, it is necessary to synthesize fNIRS-based NF training studies. Therefore, the aim of the present study was to conduct systematic review and meta-analysis of fNIRS-based NF in parallel with computerized cognitive training to investigate its clinical implication.

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2. Methods

The present study was implemented in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). This study was prospectively registered with PROSPERO (ID: CRD42021257725).

2.1. Literature search

A literature search was completed in May 2021. We searched trials investigating the effects of fNIRS-based NF training on cognitive function and activity in the PFC. This study focused on trials published from January 2011 to December 2020 using the Embase, Medline, PubMed, Web of Science, PsychINFO, and Google scholar. The following search terms were: functional near infrared spectroscopy" or "fNIRS" or "near infrared spectroscopy" or "NIRS" and "neurofeedback" or "biofeedback" and "cognitive training" or "cognitive treatment" or "cognitive intervention".

2.2. Study selection

We included all published studies on fNIRS-based NF training for improving cognitive function in healthy or patient individuals with the pre and post design that presented the results of changes in cognitive function as one of outcome measures. Considering the field related with fNIRS-based NF training is relatively young and to date randomized controlled trials have been rarely published, we adopted loose inclusion criteria including non-controlled, feasibility, pilot studies. Studies which not present cognitive domains targeted to be improved and a statistical significance were excluded. Two independent reviewers (S.Y. and J-H.) implemented the initial eligibility screening according to the titles and abstracts and then selected the studies. Disagreements between both reviewers were resolved by consultation with a third reviewer.

2.3. Eligibility criteria

2.3.1. Types of subject

As this study was not limit the specific subjects, subjects with or without cognitive impairment were included regardless of their age.

2.3.2. Types of interventions

Studies conducting fNIRS-based NF in parallel with computerized cognitive training to train one or more specific cognitive domains were included. To be included, fNIRS-based NF in parallel with computerized cognitive training had to be the primary intervention, not combined with other cognitive treatments. fNIRS-based NF in parallel with computerized cognitive training with the following sub-factors was included:

(1) fNIRS-based NF was presented in real-time according to subject's brain activity while performing computerized cognitive training.
(2) Changes in HbO2 as a fNIRS-based NF from brain regions were visually or auditorily provided on a computer monitor where cognitive training was conducted.
(3) fNIRS-based NF was presented to have subject regulate NF signals to improve their cognitive performance.
(4) Targeted ROIs of fNIRS-based NF were presented.
(5) fNIRS-based NF in parallel with computerized cognitive training was conducted for the purpose of cognitive improvement, and otherwise only adopted the judgment of clinicians.

2.3.3. Types of outcomes

The outcomes were pre- and post-test measurements of cognitive function (global cognition or specific cognitive domains).

2.4. Risk of bias and methodological quality

To investigate the risk of bias in the finally selected studies, the Risk of Bias Assessment tool for Non-randomized Study (RoBAN) with the Review Manager (RevMan) program (version 5.4.1, The Cochrane Collaboration, 2020). The methodological quality of the selected studies was evaluated with the following single-hierarchy evidence model (Table 1).[11]

2.5. Data extraction

The coding of data extracted from the finally selected studies was conducted by two independent reviewers. Extracted data included: study population and study design, ROIs, fNIRS device features, NF protocol, cognitive domains, and statistical significances. All data were coded as means, standard deviations, p-value, t-values for subject groups at pre-test and post-test.

2.6. Data analysis

The statistical heterogeneity, effect size and publication bias of the selected articles were analyzed using Comprehensive Meta-Analysis version 2.0 (Biostat, Englewood, NJ, USA). Hedges' *g* was calculated to derive the standardized mean differences. Polled of the standardized mean Hedges' *g* of < 0.30, ≥ 0.30 and < 0.60, and ≥ 0.60 indicated small, moderate, and large effect sizes, respectively. To assess statistical heterogeneity, the I^2 statistic was used and considered as low, moderate, or large at 25%, 50%, or 75%, respectively.[12] Meta-analyses were carried out using a random-effects model as the selected studies contained different subjects, designs, and outcome measures regardless of statistical heterogeneity, which could increase statistical power of meta-analyses.[13] Analyses were conducted for cognitive domains. When the selected studies included multiple measures for a certain cognitive domain, the measures were averaged to one pooled effect size. Publication bias was analyzed with funnel plots and the Egger's regression intercept test.[14] If symmetrical points on the funnel plots or the Egger's regression intercept test with a p value above 0.05 was observed, we considered that there was no publication bias.

Table 1
Single-hierarchy evidence model.

Evidence level	Study design
Level I	Systematic reviews, meta-analyses, or randomized controlled trials (RCT)
Level II	Two groups, nonrandomized studies (e.g., cohort, case-control)
Level III	One group, nonrandomized studies (e.g., before-after, pretest and posttest)
Level IV	Single-subject design or case series
Level V	Case reports or expert opinion

3. Results

3.1. Study selection

The titles and abstracts of 931 articles were screened and the full-text of the remaining 17 studies was assessed for eligibility. Four articles met the inclusion criteria were considered in the qualitative synthesis (Figure 1).

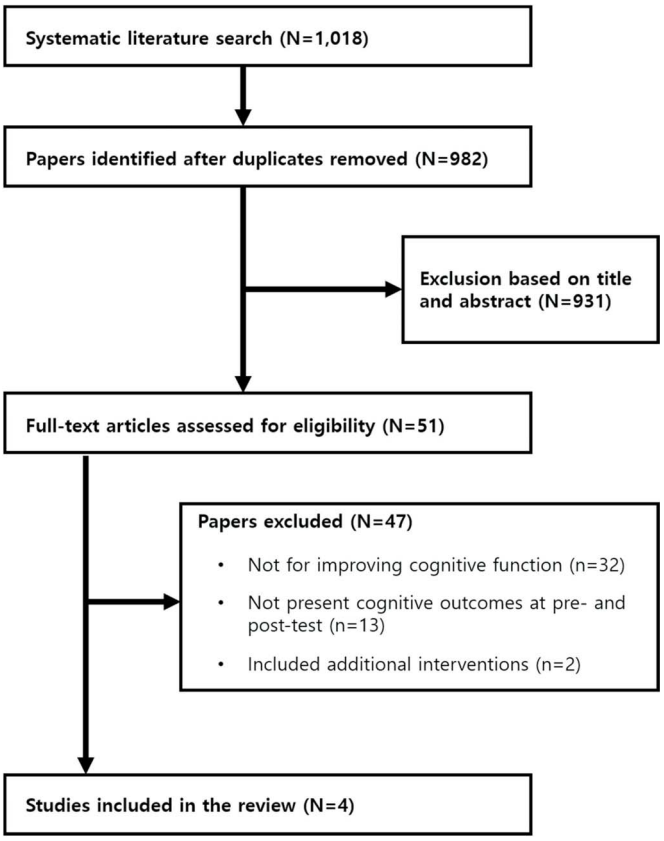

Figure 1. Flow chart of the study selection process.

3.2. Quality of the selected studies

Most of the selected studies had level II evidence level and only one study had level I evidence level (Table 1). Based on the RoBAN, except for the blinding for outcome assessment item, all studies showed low risk of bias (Figure 2).

3.3. Subject characteristics in the selected studies

The total number of included subjects was 102 and their age range between 11 and 37 years old. Subjects in three studies were healthy younger adults and one study included children with typical development and children with autistic spectrum disorder (ASD) (Table 2).

3.4. fNIRS-based NF

A number of channels ranged from 1 to 52, and as dependent variables, all studies used oxy-hemoglobin (HbO2) and one study also used deoxy-hemoglobin (HHB). ROIs which channels were attached consisted of dorsolateral prefrontal cortex (DLPFC), inferior frontal region, posterior superior temporal sulcus, and lateral orbitofrontal cortex. Immediately or delayed visual feedback on a computer screen using changes in activity from the ROIs while performing cognitive

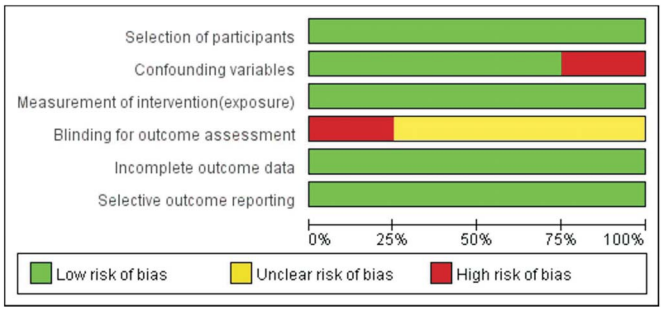

Figure 2. Risk of bias graph: authors' judgement about each risk of bias item presented as percentage across all the included studies.

Table 2
Characteristics of the studies included in the systematic review and meta-analyses.

Author and year	Subjects	fNIRS features (channel/dependent variables)	ROIs	Training session and feedback types	Targeted cognitive domains	Results	Evidence level
Hosseini et al., 2016	N = 20 (NF = 10, sham = 10), healthy younger adults	52 channels/HbO2	Right DLPFC and inferior frontal region	4 sessions (48 min), delayed visual feedback using height and color of vertical bar with an implicit strategy	Executive function and working memory	Significant decreased ROIs activity and increase in both executive function and working memory in the NF group	Level II
Liu et al., 2016	N = 4 (NF = 2, sham = 2), children with ASD (n = 2) and children with TD (n = 2)	44 channels/HbO2	Bilateral pSTS and prefrontal cortex	5 sessions (23 min), delayed visual feedback using animation of points converted to cash with an implicit strategy	Working memory	Significant decreased pSTS activity increase in working memory and in the NF group	Level II
Hudak et al., 2017	N = 20 (NF = 10, sham = 10), younger adults displaying high impulsivity	4 channels/HbO2 and HHB	Bilateral DLPFC	8 sessions (96 min), immediate visual feedback using brightness in a virtual classroom scenario with an implicit strategy	Executive function and working memory	Significant increased left DLPFC activity and improvement in executive function but not working memory in the NF group	Level I
Li et al., 2020	N = 60 (NF = 30, sham = 30), healthy younger males	12 channel/HbO2	Bilateral lateral orbitofrontal cortex	1 session (9 min), immediate visual feedback using animation of lifting a stonewith an implicit strategy	Executive function	Significant increased ROIs activity and improvement in executive function in the NF group	Level I

ASD: autism spectrum disorder, DLPFC: dorsolateral prefrontal cortex, HbO2, oxy-hemoglobin, HHB, deoxy-hemoglobin, NF: neurofeedback, pSTS: posterior superior temporal sulcus, ROIs: regions of interest, TD: typical development.

tasks were presented to the subjects and then they were instructed to regulate their activity without specific information.

To investigate effects of fNIRS-based NF training, executive function or working memory was selected as targeted cognitive domain. Two of four studies assessed both executive function and working memory (Table 2).

3.5. Meta-analysis of effects of fNIRS-based NF training

3.5.1. Overall effect on cognitive outcomes

The overall effect size was large and significant with low heterogeneity (k = 3, g = 0.682, 95% CI = 0.079 to 1.285, I^2 = 43.062) (Figure 3). The funnel plot result showed significant symmetry (Egger's intercept = 2.271, p = 0.16). This result implied that fNIRS-based NF training is helpful to improve overall cognitive function.

3.5.2. Working memory

The effect of fNIRS-based NF training on working memory was large and significant with moderate heterogeneity (k = 2, g = 1.143, 95% CI = 0.513 to 1.774, I^2 = 70.554) (Figure 4). The funnel plot showed significant symmetry (Egger's intercept = 3.143, p = 0.45). This finding indicated that fNIRS-based NF training would be effective in improving working memory.

3.5.3. Executive function

The pooled effect size of fNIRS-based NF training on executive function was moderate and significant without heterogeneity (k = 2, g = 0.406, 95% CI = 0.011 to 0.801, I^2 = 0.000) (Figure 5). The funnel plot was significant symmetry (Egger's intercept = -0.863, p = 0.68). This finding suggested that fNIRS-based NF training is beneficial to improve executive function.

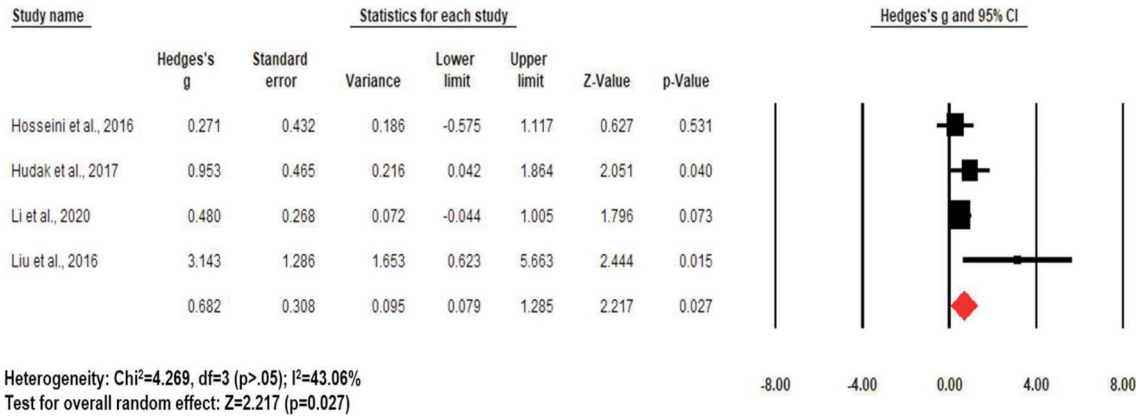

Figure 3. Forest plot demonstrating the efficacy of fNIRS-based NF training on overall cognitive function.

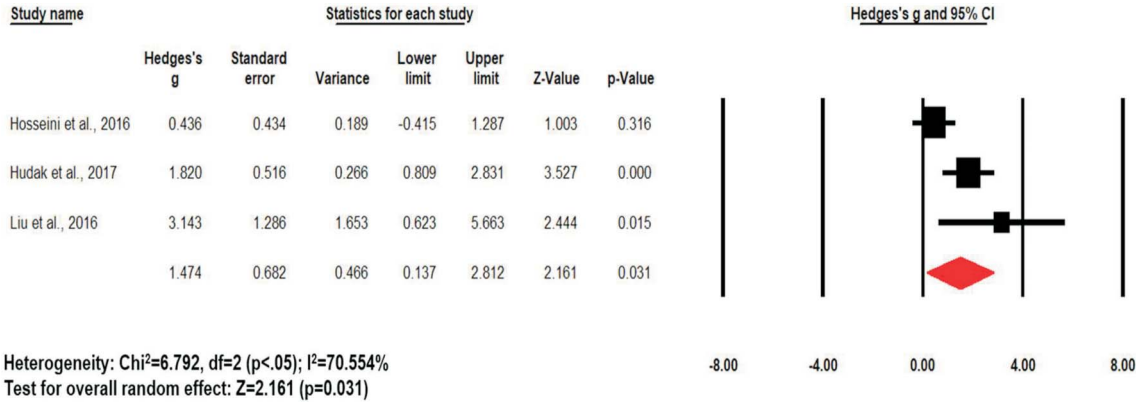

Figure 4. Forest plot indicating the efficacy of fNIRS-based NF training on working memory.

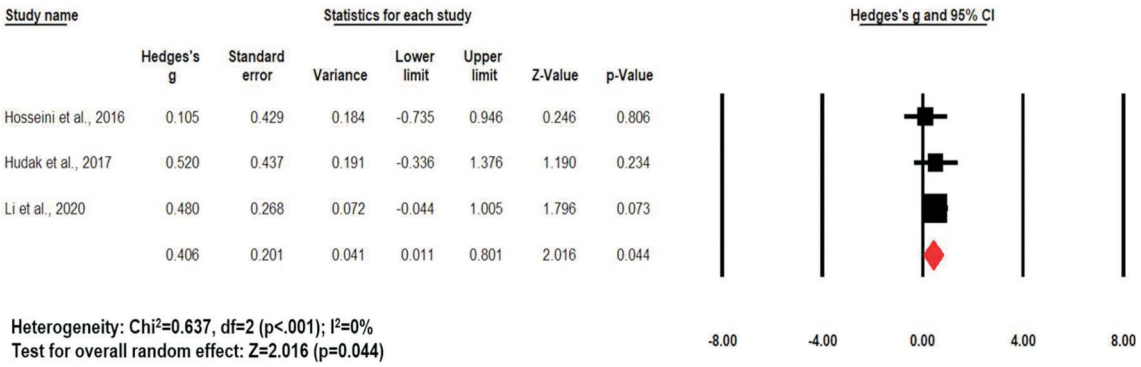

Figure 5. Forest plot showing the efficacy of fNIRS-based NF training on executive function.

4. Discussion

Based on the findings from the four articles, fNIRS-based NF training is found to be a promising intervention for improving cognitive function. There were moderate to large positive effect sizes in the cognitive outcomes, with statistical significance reached for executive function and working memory, which is in line with a previous systematic review study.[8]

This study found the fNIRS-based NF training-induced improvement in cognitive function. In four studies selected in this study,[6,15–17] fNIRS-based NF was presented to have subjects regulate their NF signals which was mostly transmitted from the PFC regions, which is consistent with a previous study reporting that the PFC is the target of the majority of fNIRS-based NF studies.[18] Since PFC function is to maintain representations of task-relevant information, regulating NF signals from the PFC which requires PFC function is sensitive to working memory.[19] Specifically, 2 out of 4 studies included the DLPFC as one of ROIs.[6,17] The DLPFC is a central component of the neural systems underlying the manipulation of verbal and visual representation in working memory, which support the present findings showing the increase in working memory by regulating the PFC.[20] On other hand, there was also a significant positive effect on executive function as well as working memory. Executive function involves a process of behavioral regulation that optimizes a goal-directed behavior outside of the domain of automatic processes. Based on Baddley's model, working memory has three components: a central executive system and two storage systems, the phonological sketch pad and the visuospatial sketchpad. The storage systems are responsible for temporarily storing verbal and visual information, where the central executive system processes information in working memory, which suggests that there is a connection between working memory and executive function.[21] In addition, a previous study found that executive function perform operation on information held in working memory so the information could be used efficiently, implying that working memory is a crucial component in executive function.[22] Indeed, neuroimaging studies commonly reported that executive function mainly depends on the PFC and a previous study indicated that fNIRS-based NF from the PFC was efficacy for improving executive function,[16,23] supporting that cognitive training using fNIRS-based NF from the PFC enhanced both working memory and executive function.

On the other hand, significant changes in activity in ROIs coupled with increased cognitive function were observed. Two out of four studies reported a significant decrease in ROIs activity, whereas the others indicated a significant increase in ROIs activity after fNIRS-based NF training. In prior studies, decreased activity in ROIs while preserving behavioral performance on cognitive tasks was found after cognitive training,[24] which could be attributed by the fact that cognitive training leads to increased PFC's neural efficiency of maintaining task-relevant information.[6,16] In other words, fNIRS-based NF training led to higher achievement with a lower amount of energy in the PFC.[24] In contrast, increased PFC activity along with improved cognitive function was also found in two studies. These studies reported that the cognitive task-specific increase in PFC oxygenation could be considered to recruit more cognitive resources from the PFC to maintain or improve cognitive task performance, which is called compensation effect.[25] This discrepancy in PFC activity between the studies selected in this study could be explained by a distinction of neural plasticity. To classify a difference in training-induced neural plasticity, a prior study introduced a distinction between patterns of redistribution and reorganization.[26] Specifically, redistribution, a pseudo-reorganization of brain activity, constitutes a combination of increase or decreases in task-specific brain areas that are associated with improvement cognitive performances after training as a demand on cognitive control increases or decreases.[26] Conversely, reorganization is considered to reflect a real change in cognitive control after cognitive training, which means that cognitive tasks could be performed neurologically differently at the beginning and end of cognitive training. Consequently, cognitive training leads to a higher neural efficiency, which is reflected in decreased activity in targeted brain regions.[10,24,26] Therefore, in two studies reporting increased activity in the PFC, it could be interpreted that fNIRS-based NF training was not sufficient to induce reorganization even though cognitive function was improved. Indeed, one of the two studies conducted fNIRS-based NF training only one session lasted 9 minutes which is less than training sessions of other two studies indicating decreased PFC activity,[17] supporting this interpretation. Although another study implemented 8 sessions' training,[16] given that subjects were younger adults showing high impulsivity, it can be said that they need a greater amount of training than healthy younger adults to induce reorganization.[16,17] In fact, a previous study found that benefits of cognitive training might be less pronounced in individual with more severe cognitive declines, supporting this interpretation.[27]

The findings of this meta-analysis study shed new light on the promising of fNIRS-based NF training for improving cognitive with slightly short periods. In addition, considering fNIRS could be used in more natural settings, compared to fMRI,[9] as it is more portable and wearable,[28] potential subjects can successfully perform cognitive training with a regulatory strategy using fNIRS-based NF at home in the absence of practitioners,[29] which has the implication of fNIRS-based NF training, compared to conventional computerized cognitive training. Furthermore, since subjects could have opportunity to have the feedback from their damaged brain regions, fNIRS-based NF training could provide personalized treatment based on neurological pattern of them. Accordingly, fNIRS-based NF training can not only standardize and provide structural cognitive training, but also control a level of training difficulty according to subject's cognitive status.[30]

The results of this study need to be interpreted in the context of limitations. First, this study could not conclude a minimum training sessions to induce improved neural efficiency, although the effect sizes on cognitive function were quite promising showing a moderate to large effects. Second, the articles selected in this study commonly adopted implicit strategies which provide no information on a certain strategy to regulate NF signals. However, explicit strategies were applied in NF studies,[15] although it has several disadvantages, especially for individuals with cognitive impairment and there is no consensus whether an instruction about NF signals should be explicit or implicit.[31] Third, due to the small number of studies and inconsistent subject characteristics including children with ASD as well as healthy subject involved in this meta-analysis, the current findings limit the generalizability of previous studies on fNIRS-based NF training. Nevertheless, considering that studies using fNIRS-based NF for the purpose of improving cognitive function have been performed recently, resulting in that the number of those is still lack, it is meaningful that the findings of this study showed clinically positive benefits of fNIRS-based NF training in the current situation. These limitations need to be addressed by conducting sub-group analysis according to subject characteristics with a large number of studies to consolidate its effects in the future. Finally, since all studies selected in this study investigate short-term cognitive outcomes, this study had insufficient data to identify long-term outcomes. Therefore, studies on long-term effects fNIRS-based NF training of need to be implemented.

5. Conclusion

This study demonstrated that fNIRS-based NF training was effective for improving working memory and executive function. Furthermore, future trials are needed to investigate long-term transfer of the efficacy of fNIRS-based NF training and its optimized training period to induce improved neural efficiency.

Acknowledgement

This work was supported by the Soonchunhyang University Research Fund.

This research was supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by Ministry of Education (No. 2021R1I1A3041487).

Conflict of Interest

The authors have no potential conflicts of interest to disclose.

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