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Differential Effects of Exercise Intensity on Brain Activity Assessed by Functional Near-Infrared Spectroscopy: A Systematic Review

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Abstract

The present systematic review aimed to provide a comprehensive understanding of the relationship between the intensity of physical activity and brain activity measured using functional near-infrared spectroscopy (fNIRS). Following the Preferred Reporting Items for Systematic Review and Meta-Analyses guidelines, studies investigating the effect of exercise intensity on brain activity were selected and summarized. Inclusion criteria were as follows: randomized controlled trial design; an adult population; physical activity; and evaluation of the effectiveness of fNIRS in assessing cognition. 11 studies were included in the analysis, 2 of which examined light-intensity exercise, 3 of which examined moderate-intensity exercise, 3 of which examined high-intensity exercise, and 3 of which compared brain activity across different intensities. Synthesis of the literature provides valuable insights into the intersection of physical activity, brain activity, and fNIRS, and contributes to a comprehensive understanding of this multifaceted relationship.

Keywords: *Exercise, Functional Near-Infrared Spectroscopy (fNIRS), Intensity, Cognition, Physical Activity*

INTRODUCTION

Regular physical activity provides significant health benefits, including improved cardiovascular, musculoskeletal, mental, and cognitive health [1]. It is associated with improved cognitive function and may account for 5%–17% of the variance in its effect on reduced utilization of healthcare resources. These associations demonstrate the cognitive benefits of regularly engaging in physical activity, which can improve overall health outcomes and potentially reduce the need for healthcare services [2]. Over the past decade, numerous studies have investigated the effects of exercise on brain function. Accumulating evidence strongly suggests that exercise improves cognition [3-5], enhances memory [6], prevents cognitive dysfunction in individuals with Parkinson's disease [7], and improves social behavior in children with attention deficit hyperactivity disorder [8] and autism [9]. Functional neuroimaging techniques have significantly enhanced the understanding of brain function in both healthy individuals and those with neurological and/or psychiatric disorders. Functional magnetic resonance imaging (fMRI), magnetoencephalography, and positron emission tomography (PET) are powerful neuroimaging tools. However, electroencephalography (EEG) and functional near-infrared spectroscopy (fNIRS) are becoming more widely used due to their portability and convenience. fNIRS has advantages over EEG, making it more suitable for everyday use owing to its higher spatial resolution, fewer physical constraints, and ability to enable free movement in a natural environment [10, 11]. Recent advances in fNIRS technology have provided insights into the neural correlates of exercise-induced cognitive changes. Although advances in neuroimaging techniques have provided new insights into the functional reorganization required for the acquisition, strengthening, and maintenance of motor skills, the optimization of exercise prescription(s) remains a challenge in cognitive motor science.

Therefore, the effects of various exercise intensities on different cognitive domains need to be clarified. However, no systematic review has evaluated intensity-specific cognitive changes. Previous research has shown that acute moderate exercise improves cognitive performance; however, the effects of acute high- and low-intensity exercise remain unclear [12-14], and studies investigating cognition and exercise intensity have reported mixed results, thus calling for a systematic review of how different exercise intensities affect neural

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activity. Understanding the varying effects of exercise intensity on cognitive processes is essential for optimizing cognitive training programs. This systematic review aimed to synthesize the existing literature regarding cognitive activation based on physical activity and exercise intensity and the utility of fNIRS in this regard. The goal was to emphasize the significance of comprehensively understanding the differential effects of exercise intensity on cognition assessed using fNIRS and to address knowledge gaps in the literature.

MATERIALS AND METHODS

This systematic review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (i.e., "PRISMA") guidelines [15]. The study protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO) (CRD42023491905).

Eligibility criteria were based on the participants, intervention, comparison, outcome, and study design (i.e., "PICOS") search tool (Table 1). Studies with healthy human adult and elderly populations (>18 years of age), without sex restrictions, were included. Furthermore, studies that used interventions with physical activity and exercise in the experimental group (e.g., aerobic, strength, combination thereof), given that brain activity had been measured using fNIRS during a cognitive test before and after a physical intervention, were also included. Randomized controlled trials (RCTs) and non-RCTs, published in English were deemed eligible for inclusion. Studies were excluded if the population consisted of patients with disorders or those using medications. Additionally, individual case studies, animal studies, and investigations that performed cognitive tests that did not measure brain activity using fNIRS were excluded.

Table 1. PICOS categories

Population	Healthy adults and elderly population, > 18 years of age
Intervention	Physical activity and exercise (light, moderate, vigorous, and near-maximal intensities)
Comparison	Baseline fNIRS-measures before the start of and/or after the physical activity and exercise or control condition
Outcomes	fNIRS
Study design	RCTs, non-RCTs (other study designs were excluded)

fNIRS, functional near-infrared spectroscopy; RCTs, randomized controlled trials

Potentially eligible, English-language studies were searched using specific keywords in three electronic databases, Medline, Scopus, and The Cochrane Library, considering studies published from January 1, 2010, to November 15, 2023. All search results were merged and uploaded to EndNote X21 (Clarivate, London, United Kingdom), and overlapping records were removed.

Two reviewers (HS and HJ) independently screened the titles and abstracts of the retrieved studies to reduce errors and avoid the risk of bias. Subsequently, the full-texts of the remaining, potentially eligible studies for inclusion and other relevant reports were examined at the full text level by the main author (HS) and one coauthor (HJ). In addition, to ensure literature saturation, the reference lists of the included articles were screened, and citations of the included studies were screened to perform backward and forward searches, increasing the likelihood of inclusion of all relevant studies. Another co-author (CS) adjudicated unclear decisions, and studies were included based on established inclusion and exclusion criteria.

The following keywords were applied individually or in combination: ("physical performance" OR exercise) AND (intensity OR load) AND ("functional near-infrared spectroscopy" OR fNIRS OR "near-infrared spectroscopy" OR NIRS OR "cortex oxygenation" OR "cognition"). Relative and absolute intensity of physical activity and exercise were classified as sedentary light, moderate, vigorous, and high (near-maximal) intensities [16, 17] (Table 2).

Table 2. Categories of exercise intensity

Intensity category	Objective measures				Subjective measure
	METs	HRmax(%)	HRR(%)	VO_2max(%)	RPE (Modified RPE)
Light	< 2.9	< 55	< 40	< 40	< 10 (<2)
Moderate	3.0-5.9	55-70	40-60	40-60	11-13 (3-4)
Vigorous	6.0-8.9	70-90	60-85	60-85	14-16 (5-6)
High (near-maximal)	≥9.0	≥90	≥85	≥85	≥17 (7)

METs : Metabolic Equivalent, HRmax : Maximal Heart Rate Reserve, HRR : Heart Rate Reserve, VO_2max : Maximal Oxygen Consumption, RPE : Rating of Perceived Exertion

Methodological quality was assessed using the Physiotherapy Evidence Database (PEDro) scale. The PEDro scale is a checklist containing 11 items, which are rated on a 2-point scale (yes = 1, no = 0) according to whether the criterion is clearly satisfied in the study, all but one of which (external validity) scores 1 point if present; therefore, the final score should range between 0 and 10 points. Quality scores were calculated for each study by adding the total scores obtained from the relevant items and dividing them by the total possible score. According to the predetermined cut-off points, study quality was classified as "high" (8 to 10), "medium" (4 to 7), or "low" (< 4) [18, 19]. The assessments were performed independently by two researchers (HS and HJ), and disagreements were resolved by consensus discussion.

RESULTS

Relevant studies were searched and selected according to the PRISMA model (Figure 1). A total of 144 studies were retrieved in the initial literature search of the 3 databases: Medline (n=53); Scopus (n=60); and Cochrane Library (n=31). Of these, 63 duplicate articles were excluded, leaving 81. Of the total number of articles, 61 were eliminated after reading the titles and abstracts, and 8 articles not retrieved were excluded. Finally, based on the eligibility criteria, 1 more study was eliminated, leaving 11 for review. Cross-checking the references of the articles in bibliographic databases did not yield any new results.

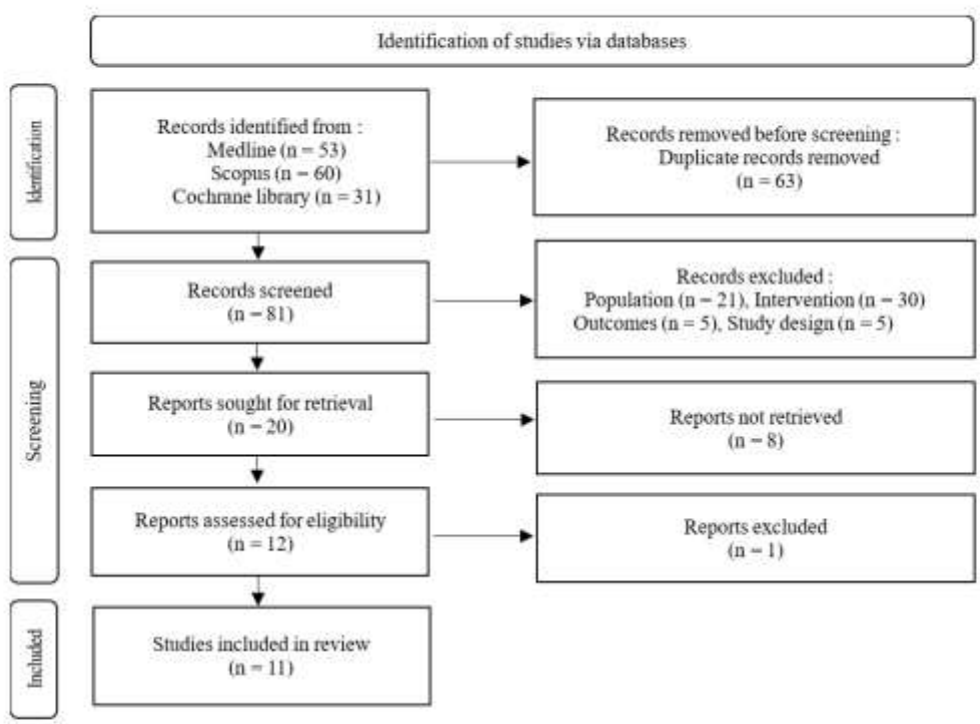

Fig. 1. Selection process for research articles (n = 11)

The methodological quality of the included studies was assessed using the PEDro scoring system. After screening the reference lists of the 11 full-text articles, 18.2% were scored as "high" and 81.8% as "medium" quality (Table 3). Two studies were of high quality [20, 21] and 9 were of medium quality [5, 22-29]. The highest scores were for the studies by Shao et al. (2023) [20] and Hu et al. (2021) [21], with scores of 8/10, while the lowest was for Byun et al. (2014b) [28], with a score of 4/10. Three RCTs described random allocation [20-22], and defined the eligibility criteria. Most of the studies performed between-group comparisons and reported score estimates and variability.

The analysis included 11 studies: 2 investigated light-intensity exercise, 3 investigated moderate-intensity exercise, 3 investigated high-intensity exercise (near-maximal), and 3 compared brain activity across different intensities (Tables 4a-c). Analysis of low-intensity protocols found an increase in oxygen-hemoglobin (oxy-Hb) from the start to end of exercise in young adults [24, 27]. However, in a study by Byun et al. (2023), a decrease in oxy-Hb was found using cycle ergometer in 30 to 50 min for 12 weeks in older adults, with no significant difference deoxy-Hb. Analysis of moderate-intensity protocols found an increase in oxy-Hb from the start to the end of exercise [5, 23-25, 28, 29]. Results from Zheng et al. (2022) supported these results and found an increase in oxy-Hb > 50% maximal oxygen uptake (VO2max) significantly increased in the prefrontal cortex (PFC), which is similar in light to moderate intensity exercise.

Investigated the effects of high-intensity exercise on cortical oxygenation [20, 21, 24-26, 28]. Results revealed that prefrontal oxy-Hb oxygenation increased until a steady-state was reached.

Table 3. Quality assessment (PEDro)

Study	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	Total score
Shao et al. (2023) [20]	1	1	1	1	1	0	0	1(100%)	1	1	1	8
Byun et al.(2023) [22]	1	1	1	1	1	0	0	0(73.7%)	1	1	1	7
Zheng et al.(2022) [23]	1	1	1	1	0	0	0	0(72.4%)	1	1	1	6
Hu et al. (2021) [21]	1	1	1	1	1	0	0	1(100%)	1	1	1	8
Zhu et al.(2021) [24]	1	1	0	1	0	0	0	0(80%)	1	1	1	5
Moriarty et al. (2019) [25]	1	1	0	1	0	0	0	1(100%)	1	1	1	6
Kujach et al.(2018) [26]	1	1	0	0	0	0	0	1(100%)	1	1	1	5
Byun et al. (2014a) [27]	1	0	0	1	0	0	0	1(100%)	1	1	1	5
Byun et al. (2014b) [28]	1	0	0	0	0	0	0	1(100%)	1	1	1	4
Hyodo et al (2012) [29]	1	0	0	1	0	0	0	1(100%)	1	1	1	5
Yanagisawa et al. (2010) [5]	1	1	1	1	0	0	0	1(100%)	1	1	1	7

The PEDro scale criteria are as follows: (1) eligibility criteria, (2) random allocation, (3) concealed allocation, (4) baseline comparability, (5) blinding of patients, (6) blinding of the therapist, (7) blinding of the assessor, (8) adequate follow-up (more than 85%), (9) intention-to-treat analysis, (10) between-group comparison, (11) point estimate and variability. The first item (eligibility criteria) is related to the external validity, and all other items are related to internal validity and interpretability. Therefore, the first item score is not added to the total score. 1 : Yes, 0 : No

DISCUSSION

In this study, we systematically reviewed the literature addressing the relationship between exercise intensity and cognitive activation during physical activity assessed using fNIRS.

This review aimed to identify variables that modulate the relationship between cognition and physical functioning to help optimize exercise programs. Based on the synthesis of eligible studies, several reported that moderate exercise promotes positive changes in cognitive performance, which is consistent with previous research [3]. Yanagisawa et al. (2010) reported that acute moderate exercise (50% VO2max) increased lateral prefrontal activation and improved cognitive performance, as measured by the Stroop test. Activation of the lateral PFC related to Stroop interference was significantly enhanced in both hemispheres, particularly in the left dorsolateral PFC, which is consistent with improved cognitive performance [5]. The International Physical Activity Guidelines recommend that older adults engage in at least 150 min of moderate-to-vigorous physical activity per week, and meeting these guidelines has been shown to improve executive function and increase oxygen delivery to the brain [30].

Although the literature suggests that inactivity is a risk factor for cognitive decline and disease, recent studies have reported that interventions involving light-intensity exercise, similar to moderate-intensity exercise, have beneficial effects on executive and cognitive functions, with enhanced cortical activation. Research has shown that light-intensity exercise can prevent age-related prefrontal volume decline and inhibit cognitive decline [31]. Additionally, acute low-intensity physical exercises, such as slow walking, yoga, and Tai Chi, can rapidly improve hippocampal memory function by strengthening the functional connections between the DG/CA3 and neocortical areas [32]. Short, light exercise at 30% VO2max for 10 min improved executive function by increasing neural activation in task-related prefrontal sub-regions in young adults through a motor-controlled arousal system [33]. Long-term light exercise interventions have also been shown to improve executive function in middle-age and particularly older adults, by modulating neural efficiency in the PFC [22]. However, it has been suggested that a higher exercise intensity is necessary to elicit central changes in brain activity. This is particularly important in clinical populations with neurological and neurodegenerative disorders [34]. This study analyzed neural activity in the PFC during dual-tasking (DT) at varying exercise intensities. The results revealed that in the low-intensity condition, PFC activity increased only after DT. This suggests that PFC activity may be beneficial for older adults or those unable to perform high-intensity exercise [13]. These findings are valuable because lighter exercises are easier to perform repeatedly in daily life for sedentary young individuals and older adults, as well as for those with medical conditions that prevent them from performing high-intensity exercise. Additionally, the addition of low-intensity, dual-task exercises should positively affect cognitive function.

According to literature, high-intensity exercise has been linked to lower processing speed and fluid cognition scores. Additionally, various high- and moderate-intensity protocols have resulted in small differences in executive function [24, 25]. This suggests that exercise(s) that induce fatigue may negatively affect subsequent cognitive processes [25].

However, Shao et al. (2023) found changes in the activation patterns in the dorsolateral and ventral PFCs in both high-intensity interval training (i.e., “HIIT”) and Tabata groups. This suggests that prolonged high-intensity exercise can lower basal heart rate, improve executive function, and increase the body's central tolerance to fatigue and stress stimuli [20]. Hu et al. (2021) presented evidence that short-term HIIT can modify cortical plasticity and execution-related cortical activation. This highlights the significance of short-term physical training in enhancing neuroplasticity [21]. This evidence supports the hypothesis that HIIT may help counteract the negative effects of aging on cognition and reduce the risk for future cognitive impairment by improving executive function in the short term. Furthermore, improvements in executive function induced by HIIT are maintained for a significantly longer period after exercise than those induced by moderate-intensity, continuous exercise [35, 36]. These findings suggest that intermittent HIIT can serve a purpose for individuals with limited exercise time and promote healthier lifestyles. However, it is important to consider fitness levels and fatigue triggers.

The present study had some limitations because it only included healthy adults ≥ 18 years of age and did not consider factors, such as DT, to enhance cognitive function. Further research is required to determine the appropriate exercise intensity for individuals with medical conditions. Additionally, a systematic review should be performed to develop tests for physical activity and cognitive improvements. Nevertheless, this study is important because, to our knowledge, it was the first to explore exercise intensity as a component of exercise prescriptions for adults without physical limitations caused by specific medical conditions. This systematic review emphasizes the crucial role of exercise intensity in shaping brain activation and functional connectivity. This suggests that intense physical activity has beneficial effects in healthy adults. High-intensity exercise, such as Tabata or HIIT, is recommended for pain-free adults with limited leisure time, whereas low-intensity exercise is recommended for physically inactive individuals to maintain or improve physical and cognitive health.

CONCLUSION

In summary, results of this study highlight the critical importance of exercise intensity in shaping brain activation and functional connectivity, thus informing future cognitive research investigating young and older adults.

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Table 4a. Overview of the results

Authors (year)	Characteristics of participants (age, Mean ± SD)	Interventions		Outcomes measured fNIRS - devise, task, IOD, wave, specifications	Outcomes
		Type (duration)	Intensity		
Shao et al. (2023) [20]	Young adults (19.4 ± 1.4 years, 21M/21F, n = 42) HIIT n = 14 TG n = 15 CG n = 13	Cycle ergometer HIIT(12min) TG(12min)	HIIT : High intensity 80-95% HRmax	Portable Brite Artinis fNIRS version 24 Brain imaging system (Artinis Medical Systems, Netherlands) Stroop task IOD : 3cm 2 wave lengths : 760 and 850 nm	· HIIT : oxy-Hb↑(R-DLPFC, R-VLPFC) · TG vs CG : oxy-Hb no significant
Byun et al. (2023) [22]	Older adults (mean 68.2 years, 20M/61F, n = 81) EG n = 40 CG n = 41	Cycle ergometer (3 sessions/week, 30-50 min/session,12 weeks)	Light intensity 35% VO_2peak	Multichannel fNIRS optical topography system ETG-7000 (Hitachi Medical Corporation, Japan) Stroop interference IOD : 3cm 2 wave lengths : 785 and 830 nm	· oxy-Hb↓, SI-related RT
Zheng et al. (2022) [23]	Young adults (22.7 ± 3.4 years, 12M/15F, n = 21)	Cycle ergometer EG (15min, 7 days) CG : Sitting condition (without exercise)	Moderate intensity 64–76% HRmax	Multichannel continuous-wave fNIRS system (NIRSport 2; NIRx Medical Technologies, United States) n-back task IOD : 3cm 2 wave lengths : 760 and 850 nm	· EG vs CG : oxy-Hb↓ (bilateral frontopolar area, DLPFC, .R-premotor and supplementary cortex)
Hu et al. (2021) [21]	Young adults (19.2 ± 0.6 years, 32F, n = 32) EG n = 16 CG n = 16	Cycle ergometer HIIT : 25min, 4 times/week CG : normal lifestyle without training	HIIT : High intensity 3 min - 50% HRR 2 min - 90% HRR	Continuous wave-NIRS system (NIRSIT, OBELAB, South Korea) Stroop Task IOD : 3cm 2 wave lengths : 760 and 850 nm	· HIIT vs CG : ICF↓, DLPFC↑, /OFC no significant

fNIRS : Functional Near-Infrared Spectroscopy, IOD : Inter Optode Distance, M : Male, F : Female, HIIT : High-Intensity Interval Training, TG : Tabata Group, CG : Control Group, HRmax : Maximal Heart Rate Reserve, oxy-Hb : Oxygenated Hemoglobin, deoxy-Hb : Deoxygenated Hemoglobin, total-Hb : Total Hemoglobin, R : Right, DLPFC : Dorsolateral Prefrontal Cortex, , EG : Experimental Group, VO_2peak : Peak Oxygen Uptake, O_2Hb : Oxyhemoglobin, SI : Stroop Interference, RT : Reaction Time, HRR : Heart Rate Reserve, ICF : Intracortical Facilitation, OFC : Orbitofrontal Cortex

Table 4b. Overview of the results

Authors (year)	Characteristics of participants (age, Mean ± SD)	Interventions		Outcomes measured fNIRS - devise, task, IOD, wave specifications	Outcomes
		Type (duration)	Intensity		
Zhu et al. (2021) [24]	Young adults (21.0 ± 1.7 years, 20M, n = 16)	MICR, MICC (40min) HIIR, HIIC (33min)	· MICR, MICC : Moderate intensity 60% VO_2max · HIIR, HIIC : High intensity 5 min - 60% VO_2max & 4 trials (4 min - 90% VO_2max, 3 min - 60% VO_2max)	The cerebral fNIRS applies the modified Beer-Lambert Law Flanker task IOD : 3.5cm 2 wave lengths : 760 and 850 nm	· Pre-test < Post-test : O_2Hb↑ (L- DLPFC)
Moriarty et al. (2019) [25]	Adults (35.0 ± 5.0 years, 4M/4F, n = 8)	Cycle ergometer MIE (45min) HIE (45min) Mind-body yoga exercise YE (45min)	· MIE : Moderate intensity 50% VO_2max RPE 13 · HIE : High intensity 85–95% VO_2max RPE 17 · YE : RPE 9	fNIRS system (OctaMon, Artinis Medical Systems, Elst, The Netherlands) NIH Toolbox Fluid Cognition assessment IOD : 3cm 2 wave lengths : 760 and 850 nm	· MIE ↑ vs CG, HIE, YE : Hbdiff ↑ (L-PFC) · HIE, MIE, and YE, Pre-test vs Post-test : Hbdiff ↑ (L-PFC and R-PFC
Kujach et al. (2018) [26]	Young adults (21.0 ± 1.6 years, 16M/9F, n = 25)	Cycle ergometer HIE (10min) CG (10min)	HIE : High intensity 60% MAP	NIRSport (NIRx Medical Technologies, LLC, Glen Head, NY, USA) Color-word matching Stroop task IOD : 3cm 2 wave lengths : 760 and 850 nm	· HIE : oxy-Hb ↑ (L-DLPFC) / deoxy-Hb no significance
Byun et al. (2014a) [27]	Young adults (20.6 ± 1.0 years, 13M/12F, n = 25)	Cycle ergometer EG(10 min) CG (10 min, without exercise)	Light intensity 30% VO_2peak	Multichannel fNIRS optical topography system ETG-7000 (Hitachi Medical Corporation, Japan) Color-word matching Stroop task IOD : 3cm 2 wave lengths : 785 and 830 nm	· EG vs CG : oxy-Hb ↑ / c no significance

fNIRS : Functional Near-Infrared Spectroscopy, IOD : Inter Optode Distance, M : Male, F : Female, MICR : Moderate-Intensity Continuous Running, MICC : Moderate-Intensity Continuous Cycling, HIIR : High-Intensity Intermittent Running, HIIC : High-Intensity Intermittent Cycling, VO_2max : Maximal Oxygen Consumption, O_2Hb : Oxyhemoglobin, L : Left, R : Right, DLPFC : Dorsolateral Prefrontal Cortex, MIE : Moderate Intensity Aerobic Exercise, HIE : High Intensity Aerobic Interval Exercise, YE : Mind-Body Yoga Exercise, CG : Control Group, Hbdiff : Oxyhemoglobin Difference, PFC : Prefrontal Cortex, oxy-Hb : Oxygenated Hemoglobin, deoxy-Hb : Deoxygenated Hemoglobin, EG : Experimental Group, VO_2peak : Peak Oxygen Uptake

Table 4c. Overview of the results

Authors (year)	Characteristics of participants (age, Mean ± SD)	Interventions		Outcomes measured fNIRS - devise, task, IOD, wave specifications	Outcomes
		Type (duration)	Intensity		
Byun et al. (2014b) [28]	Young adults (20.3 ± 1.7 years, 5M/9F, n = 14)	Cycle ergometer EG (10 min)	· Light intensity 30% VO_2peak · Moderate intensity 50% VO_2peak · High intensity 70% VO_2peak	MCA Vmean (WAKI 1-TC; Atys Medical, France)	· Pre-test vs Post-test : SBFv and HR ↑ / MCA Vmean no significance
Hyodo et al (2012) [29]	Older adults (69.3 ± 3.5 years, 28M/5F, n = 33)	Cycle ergometer EG (Ex 10min + rest 15 min) CG (rest 25 min)	Moderate intensity 50% VO_2max	Multichannel fNIRS optical topography system ETG- 7000 (Hitachi Medical Corporation, Kashiwa, Japan) Stroop Task IOD : 3cm 2 wave lengths : 785 and 830 nm	· EG vs CG : oxy-Hb ↑ (L-DLPFC)
Yanagisawa et al. (2010) [5]	Young adults (21.5 ± 4.8 years, 17M/3F, n = 20)	Cycle ergometer EG (Ex 10min + rest 15 min) CG (rest 25 min)	Moderate intensity 50% VO_2peak	Multichannel fNIRS optical topography system ETG- 7000 (Hitachi Medical Corporation, Kashiwa, Japan) Stroop Task IOD : 3cm 2 wave lengths : 785 and 830 nm	· Pre-test vs Post-test : oxy-Hb ↑ (L-DLPFC)

fNIRS : Functional Near-Infrared Spectroscopy, IOD : Inter Optode Distance, M : Male, F : Female, EG : Experimental Group, VO_2peak : Peak Oxygen Uptake, MCA Vmean : Middle Cerebral Artery Mean Blood Velocity, Ex : Exercise, SBFv : Skin Blood Flow Velocity, HR : Heart Rate, CG : Control Group, VO_2max : Maximal Oxygen Consumption, oxy-Hb : Oxygenated Hemoglobin, L : Left, DLPFC : Dorsolateral Prefrontal Cortex