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Original Article

The characteristics of cerebral cortical oxygenation levels and functional connectivity under upper and lower limb exercise-induced fatigue

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ABSTRACT

This study aims to explore the impact of fatigue induced by different limb exercises on cerebral cortical oxygenation levels and functional connectivity strength using functional near-infrared spectroscopy (fNIRS). Fatigue was induced using an upper limb ergometer or a lower limb ergometer, with the load increasing gradually each minute. fNIRS covering the prefrontal cortex and motor cortex were used to collect data during the resting state, both before and after fatigue induction. A two-way ANOVA was conducted to examine differences in oxyhemoglobin (HbO_2) and functional connectivity before and after fatigue induction in both groups, with the significance level set at 0.05. Exercise-induced fatigue in both the upper and lower limbs leads to a significant decrease in cerebral cortical oxygenation levels. Upper limb fatigue leads to a significant reduction in functional connectivity, there were significant decreases in connectivity within the motor cortex, between the motor cortex and frontal regions, and between the right ventrolateral prefrontal cortex and other frontal regions. Conversely, no significant changes were observed before and after lower limb fatigue. Future studies should focus on examining the extent to which how changes in the cerebral cortex, induced by exercise fatigue, are linked to exercise- and/or performance-related outcomes.

List of Abbreviation:

DLPFC	Dorsolateral Prefrontal Cortex
EF	Exercise-Induced Fatigue
fNIRS	Functional Near-Infrared Spectroscopy
FPA	Frontopolar Area
HbO_2	Oxyhemoglobin
HHb	Deoxyhemoglobin
LDLPFC	Left Dorsolateral Prefrontal Cortex
LFPA	Left Frontal Pole Area
LLEF group	Lower Limb Exercise-Induced Fatigue Group
LM1	Left Primary Motor Cortex
LOFA	Left Orbitofrontal Area
LPM	Left Premotor and Supplementary Motor Cortex
LS1	Left Primary Somatosensory Cortex
LVLPFC	Left Ventrolateral Prefrontal Cortex
M1	Primary Motor Cortex
OFA	Orbitofrontal Area
PFC	Prefrontal Cortex
RDLPFC	Right Dorsolateral Prefrontal Cortex
RFPA	Right Frontal Pole Area
RM1	Right Primary Motor Cortex
ROFA	Right Orbitofrontal Area
ROI	Region of Interesting
RPE	Rating of Perceived Exertion
RPM	Right Premotor and Supplementary Motor Cortex
RS1	Right Primary Somatosensory Cortex
RVLPFC	Right Ventrolateral Prefrontal Cortex
S1	Primary Somatosensory Cortex
ULEF group	Upper Limb Exercise-Induced Fatigue Group
VLPFC	Ventrolateral Prefrontal Cortex

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1. Introduction

Exercise-induced fatigue (EF) is a common physiological phenomenon in athletic training and a key factor limiting athletic performance.[1] Understanding the mechanisms of EF is crucial for delaying its onset and promoting recovery. Research suggests that EF is caused by both central and peripheral factors.[2] Central fatigue involves a loss of force or strength originating near the neuromuscular junction and is related to the

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reduction in motor neuron frequency and motor cortex drive.[3] Peripheral fatigue results from decreased function beyond the neuromuscular junction, such as reduced muscle fiber contraction strength or changes in the transmission mechanism of muscle action potentials.[4] During fatigue, the peripheral system and the central nervous system interact through metabolic and neurochemical pathways involving the skeletal muscles, spinal cord, and brain.[5]

In recent years, with the popularization and development of sports dominated by upper limbs or both upper and lower limbs, such as wheelchair sports and rock climbing, researchers have become increasingly interested in the effects of EF in different limbs.[3,6] Studies have found that upper limb fatigue has a greater impact on athletic performance compared to lower limb fatigue, such as a more significant decline in balance ability following upper limb fatigue.[7–9] It is well known that there are differences between the upper and lower limbs in terms of the nervous system, such as the proportion of limb projection in the brain[10] and brain activation during activities.[11] Previous research has shown significant differences in brain oxygenation levels during incremental load exercises of the upper and lower limbs, with the oxygenation level being significantly higher in the upper limbs at peak power.[12] Additionally, studies have found that central fatigue is greater after knee extensor fatigue compared to elbow flexor fatigue, while peripheral fatigue and corticospinal inhibition are smaller.[13] The "central control model" theory posits that fatigue is the result of the central motor nervous system actively regulating motor unit neural control commands based on sensory input from peripheral organs and brain tissue itself.[14] Although there has been attention to the impact of limb-specific EF from both central and peripheral perspectives,[15–19] there is still insufficient evidence on the central effects of upper and lower limb fatigue. Therefore, further exploration of these differences is crucial for a comprehensive understanding of EF.

The impact of EF on athletic performance varies between different limbs, and observing this from the perspective of the central nervous system may be particularly crucial. Functional near-infrared spectroscopy (fNIRS) can continuously monitor changes in the concentrations of oxygenated and deoxygenated hemoglobin in the cerebral cortex, reflecting the brain's metabolic activity and functional state.[20] By analyzing cortical functional connectivity, fNIRS can reveal the interactions and information exchange between cortical regions under fatigue.[20–22] Therefore, this study aims to investigate the differences in the effects of upper and lower limb EF on the cerebral cortex. By using fNIRS to obtain and compare indicators of brain oxygenation levels and functional connectivity strength in healthy participants at rest and after experiencing limb fatigue. This research seeks to provide supporting evidence for related studies in this field.

2. Materials and methods

2.1. Ethical approval

Written informed consent was obtained from all the participants prior to data collection. This study was reviewed and approved by the Ethics Committee of Shanghai University of Sport in accordance with the Declaration of Helsinki (NO.102772023RT031).

2.2. Participants

This study employs a randomized, controlled design and recruited 60 participants (effect size = 0.25; power = 0.80; $\alpha = 0.05$). The inclusion criteria were: (1) age between 18 and 28 years; (2) regular exercise habits, defined as exercising more than three times a week for over six months; and (3) right-hand dominance. The exclusion criteria were: (1) history of sports injuries or surgeries within the past six months; (2) history of any disease affecting physical activity; and (3) use of psychiatric or neurological medications in the past six months. The participants' basic information is presented in Table 1. Before testing, participants were familiarized with the experimental protocol and signed an informed consent form.

Table 1
Participants' basic information.

Sample size (*n*)	Sex (men/women)	age (years old)	height (cm)	weight (kg)
ULEF group (n = 30)	14/16	23.13 ± 2.87	169.38 ± 8.34	61.60 ± 12.85
LLEF group (n = 30)	14/16	23.27 ± 2.82	170.23 ± 6.71	63.33 ± 15.23
t	–	−0.017	−1.053	−1.431
p	–	0.986	0.297	0.158

ULEF group: upper limb exercise-induced fatigue group; LLEF group: lower limb exercise-induced fatigue group.

2.3. Study design

This study was a randomized controlled design. Sixty subjects were randomly divided into upper limb exercise-induced fatigue group (ULEF group) and lower limb exercise-induced fatigue group (LLEF group). Before the experiment, the researchers recorded the participants' basic information and explained the experimental procedure and precautions to them. They were instructed to avoid strenuous exercise, staying up late, and consuming caffeine or alcohol within 24 hours (h) before the experiment.

2.3.1. Upper limb exercise-induced fatigue group

The participants sat on a chair with their feet flat on the ground, facing the bicycle. The bicycle was aligned with their body midline, and the seat position was adjusted according to their arm length. They completed a 3-minute (min) warm-up on an upper limb ergometer (Monark 891E, Sweden) at a self-selected pace. Upper limb fatigue was induced using an incremental load exercise protocol.[23] The exercise started with zero load, increasing by 0.2 kg every minute. Participants were instructed to maintain a speed of 90 revolutions per minute (rpm) and to exert maximum effort until the exercise ended. Heart rate and the Borg Rating of Perceived Exertion (RPE) were recorded every minute.[24,25] Exercise-induced fatigue was determined when the participants reported an RPE of 18 or higher and were unable to maintain the speed for more than 5 seconds (*s*).[26] After reaching fatigue, participants rested while remaining seated (Fig. 1 A).

2.3.2. Lower limb exercise-induced fatigue group

The participants sat on a power bicycle, with the seat height adjusted according to the participant's leg length and the handlebar distance adjusted based on arm length. This setup ensured that the upper body remained upright and stable, preventing any pulling on the fNIRS device's optical fibers during exercise. Participants completed a 3-min warm-up on a lower limb ergometer (Monark 839E, Sweden) at a self-selected pace. Lower limb fatigue was induced using an incremental load exercise protocol.[27] The exercise started with zero load, increasing by 25 W every minute. Participants were instructed to maintain a speed of 60 rpm and to exert maximum effort until the exercise ended. The criteria for determining fatigue were the same as those used for the upper limb fatigue group (Fig. 1 B).

2.4. Data collection

While seated, participants were equipped with a fNIRS device (NIRScout, NY) and a heart rate monitor (Polar H10, Finland). The fNIRS monitored areas included the prefrontal cortex and motor regions. The spatial positions of the channels were registered to standard space coordinates based on the Montreal Neurological Institute (MNI) method (Fig. 2).[28] Seven regions of interest (ROIs) were selected based on the Brodmann cortical area system, including the primary motor cortex,

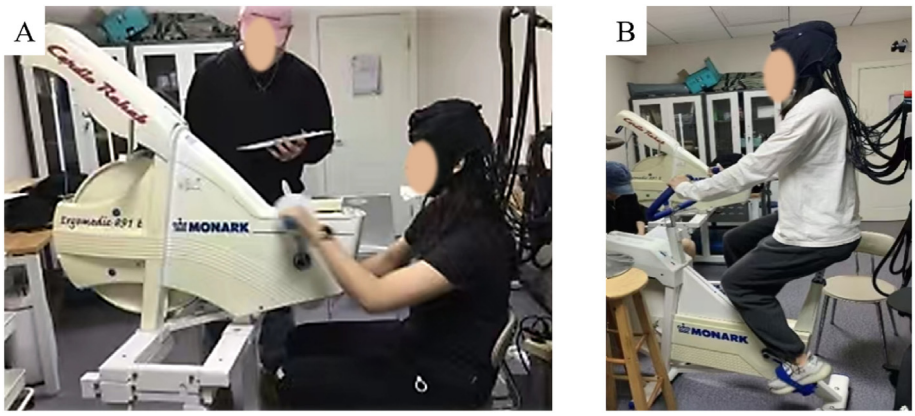

Fig. 1. Experimental setup diagram. (A) shows upper limb exercise induced fatigue, and (B) shows lower limb exercise induced fatigue.

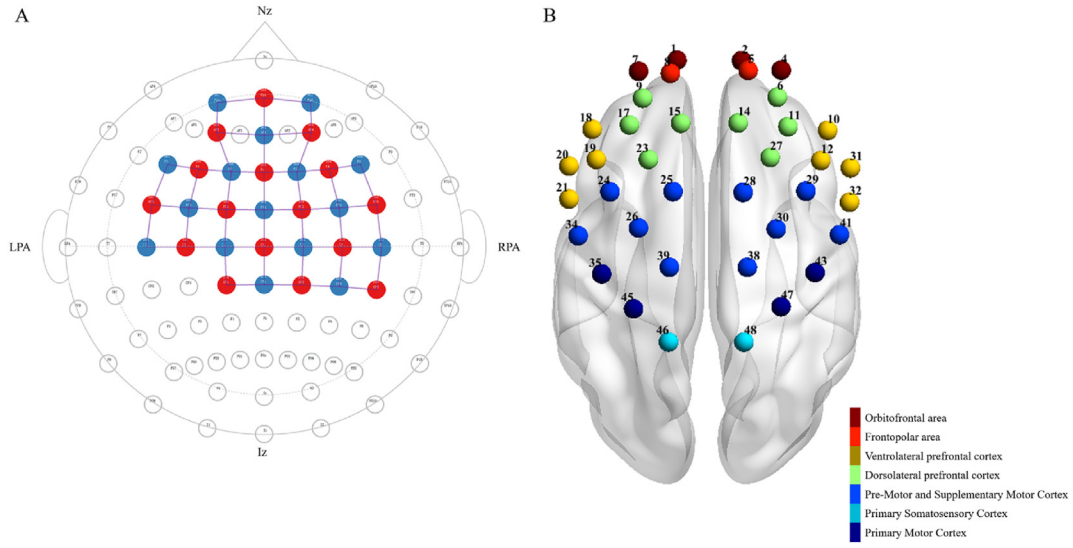

Fig. 2. The fNIRS monitored areas. (A) shows schematic diagram of fNIRS monitoring probes and channel distribution. Red circles represent light sources, blue circles represent detectors, and the lines represent channels. (B) The different colors in the figure represent different brain regions of interest.

premotor and supplementary motor cortex, primary somatosensory cortex, dorsolateral prefrontal cortex, ventrolateral prefrontal cortex, frontal pole, and orbitofrontal area. Resting-state brain activity was collected before and after the fatigue task, with participants remaining seated for 5 min.

2.5. Data processing

2.5.1. Data preprocessing

Data preprocessing was conducted using Homer2 in MATLAB (R2017a, MathWorks, USA). The main steps included: Converting raw light intensity to optical density. Identifying and removing artifacts using the hmrMotionArtifactByChannel function, which marked data points as artifacts (along with the surrounding 2 s) if fluctuations exceeded three times the mean or 30 times the standard deviation within 1 s. Artifacts were corrected using the hmrMotionCorrectSpline function. Poorly corrected artifacts were re-identified using the same criteria and marked for exclusion. If an artifact could not be corrected or resulted from excessive head movement, the entire dataset for that channel was excluded.[29] Applying band-pass filtering to eliminate noise and low-frequency drift, with a high-pass cutoff frequency of 0.01 Hz and a low-pass cutoff frequency of 0.1 Hz. Converting optical density to concentrations of oxyhemoglobin (HbO_2) and deoxyhemoglobin (HHb) using the modified Beer-Lambert law. For subsequent analyses, only HbO_2 concentration data were used due to its higher signal-to-noise ratio.

2.5.2. Calculation of oxygenation levels

Data processing was performed in MATLAB. First, resting-state data segments before and after exercise were extracted for each dataset. Then, HbO_2 concentration values corresponding to the ROI channels were extracted and averaged across channels. Finally, the time series average of HbO_2 concentration was calculated for each ROI.

2.5.3. Calculation of functional connectivity

The most common method for studying brain functional connectivity is correlation analysis,[30] which evaluates the connectivity between different brain regions by calculating their correlations. Pearson correlation analysis was used to compute the correlation coefficients (r) between each pair of ROIs, resulting in correlation matrices for the resting state and the post-fatigue resting state. These correlation matrices were then transformed into z-value matrices using Fisher-Z transformation to achieve normalization and standardization of the data.

2.6. Statistical analysis

Statistical analyses were performed using SPSS 27.0 (IBM, USA). The Shapiro-Wilk test was used to check the normality of the data. If the data followed a normal distribution, they were presented as "mean ± standard

deviation" and analyzed using parametric tests. An independent samples *t*-test was used to compare differences in basic information, exercise duration, heart rate, and RPE between the two groups. Two-way ANOVA was employed to compare differences before and after fatigue as well as between the two exercise modes. If an interaction effect was found, a simple effects analysis was conducted. If a main effect was found, paired samples *t*-tests were used to analyze differences before and after fatigue. Multiple comparisons were corrected using the false discovery rate (FDR). The significance level was set at $\alpha = 0.05$. Cohen's *d* was used to represent the effect size: < 0.10 indicates a negligible effect, 0.10–0.30 indicates a small effect size, 0.30–0.50 indicates a moderate effect size, and > 0.50 indicates a large effect size.[31]

3. Results

3.1. Physiological indicators

The physiological indicators of participants at the end of exercise are shown in Table 2. All participants reported feeling "exhausted" at the end of the exercise, with RPE levels above 18, and were unable to continue. Due to poor signal quality in the fNIRS data, 6 participants were excluded from further analysis. Consequently, the upper limb test group included 28 participants, and the lower limb test group included 26 participants.

3.2. Changes in blood oxygen levels

Two-way ANOVA revealed no significant interaction effect between the two limb exercise modes on blood oxygen levels ($F = 1.60$, $p = 0.092$), and no significant group effect ($F = 1.42$, $p = 0.158$). However, there was a significant main effect of time ($F = 2.12$, $p = 0.018$). Paired samples *t*-tests were used to compare within-group differences, showing that brain blood oxygen levels significantly decreased after both upper and lower limb exercise-induced fatigue (Fig. 3).

3.2.1. Blood oxygen levels before and after ULEF

Statistical analysis revealed significant changes in HbO_2 in several brain regions following upper limb exercise-induced fatigue. Specifically, HbO_2 levels significantly decreased in the left primary motor cortex, bilateral dorsolateral prefrontal cortices, left ventrolateral prefrontal cortex, right frontal pole, and bilateral orbitofrontal cortices (Table 3).

3.2.2. Blood oxygen levels before and after LLEF

Statistical analysis revealed significant changes in HbO_2 in certain brain regions following lower limb exercise-induced fatigue. Specifically, HbO_2 levels significantly decreased in the left premotor and supplementary motor cortex, as well as in the bilateral dorsolateral prefrontal cortices (Table 4).

3.3. Changes in functional connectivity

Two-way ANOVA indicated that there was no significant interaction effect between the two limb exercise modes on functional connectivity strength ($F = 2.60$, $p = 0.107$), and no significant group main effect ($F = 3.52$, $p = 0.061$). However, there was a significant main effect of time ($F = 4.1$, $p = 0.043$). Paired samples *t*-tests showed that the changes in functional connectivity strength before and after fatigue were significant for the upper limb exercise mode, whereas the changes for the lower limb exercise mode were not significant.

Table 2
Physiological measures at the end of the exercise.

Group	Time (*s*)	RPE_{max}	HR_{max} (bpm)
ULEF group ($n = 28$)	503.68 ± 64.38	19.42 ± 0.69	169.5 ± 10.98
LLEF group ($n = 26$)	618.38 ± 81.96	19.46 ± 0.70	177.38 ± 8.31
t	−5.741	−0.174	−2.987
p	**< 0.001**	0.867	**0.004**

ULEF group: upper limb exercise-induced fatigue group; LLEF group: lower limb exercise-induced fatigue group. Bold values in the table indicate statistical significance; $t < 0$ indicates ULEF group < LLEF group, $t > 0$ indicates ULEF group > LLEF group; RPE: Rate of Perceived Exertion; HR: Heart Rate; bpm: beats per minute.

3.3.1. Functional connectivity before and after ULEF

Pearson correlation analysis revealed the functional connectivity states between brain regions before and after fatigue induction during the resting state (see Fig. 4). Paired *t*-test analysis, with corrections applied, indicated a significant decrease in functional connectivity strength across most regions following exercise-induced fatigue. Specifically, there was a notable reduction in connectivity strength within the motor cortex (primary motor cortex, premotor and supplementary motor areas, primary somatosensory cortex) and between the motor cortex and frontal lobe regions (bilateral dorsolateral prefrontal cortices, bilateral ventrolateral prefrontal cortices, bilateral frontal poles, bilateral orbitofrontal cortices). Additionally, the connectivity strength between the right ventrolateral prefrontal cortex and the left ventrolateral prefrontal cortex, right dorsolateral prefrontal cortex, and right frontal pole also significantly decreased.

3.3.2. Functional connectivity before and after LLEF

Pearson correlation analysis revealed the functional connectivity states between brain regions before and after fatigue induction during the resting state (see Fig. 5). Paired *t*-test analysis indicated increased functional connectivity strength between the left dorsolateral prefrontal cortex and the left orbitofrontal cortex, as well as the left frontal pole. Additionally, increased connectivity was observed between the left orbitofrontal cortex and bilateral frontal poles. However, these changes were not statistically significant after correction.

4. Discussion

This study investigated changes in cortical blood oxygen levels and brain functional connectivity characteristics before and after upper and lower limb exercise-induced fatigue. The findings revealed that participants experienced significant physiological changes, alterations in brain oxygenation, and modifications in network connectivity following exercise-induced fatigue.

4.1. Heart rate and RPE after exercise-induced fatigue

Participants in this study reported their RPE levels as "very hard" or "exhausted" at the end of both upper and lower limb exercises, aligning with previous fatigue research,[32] which noted that the most intense fatigue typically occurs at the conclusion of exercise. This indicates that the fatigue induction in this study was effective as expected. The average heart rate at the end of exercise was 169 bpm for the upper limb fatigue group and 177 bpm for the lower limb fatigue group. Consistent with previous studies, heart rates during upper limb fatigue were lower than those during lower limb fatigue.[17,33,34] This physiological difference may be attributed to variations in muscle tissue composition; upper limb muscles contain about 30% type I fibers compared to approximately 50% in lower limb muscles.[35] Additionally, upper limb cycling recruits more type II fibers, which have lower metabolic efficiency.[33,34] Furthermore, the muscle mass involved in lower limb cycling is significantly greater than that in upper limb cycling, requiring more blood supply.[36] Consequently, the relatively smaller muscle mass and lower metabolic efficiency in upper limb exercise result in a lower heart rate, as the cardiovascular load is less. In contrast, the increased demand for blood in large muscle groups during lower limb exercise leads to higher heart rates.[36] These findings indicate that different limb exercises impose varying levels of cardiovascular stress.

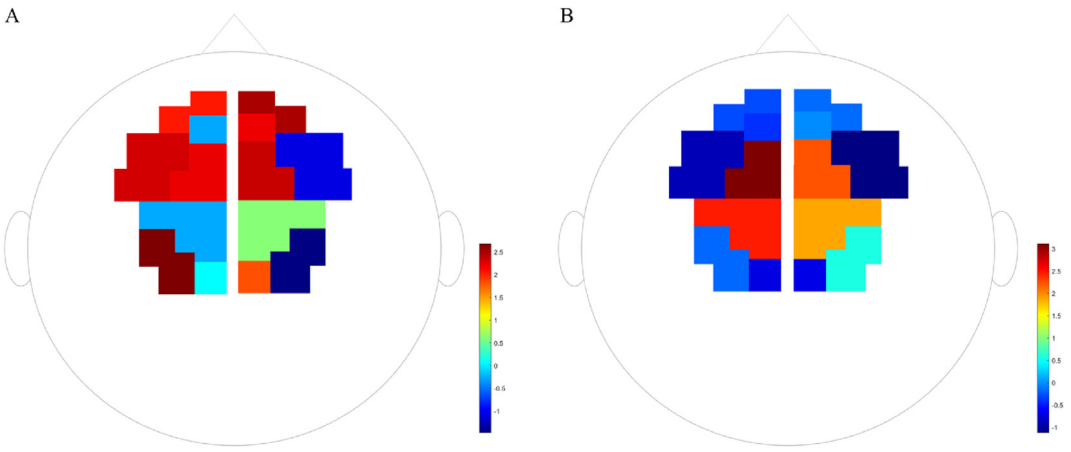

Fig. 3. Changes in oxygenation levels before and after exercise-induced fatigue. (A) displays the differences in oxygenation levels before and after upper limb fatigue. (B) shows the differences in oxygenation levels before and after lower limb fatigue. The color bar represents the *t*-values of the differences, with larger *t*-values indicating greater differences. Red indicates oxygenation levels were higher before fatigue, while blue indicates oxygenation levels were lower before fatigue.

Table 3
Brain regions with HbO_2 differences before and after upper limb fatigue.

Brain region	Resting State Before Fatigue (Mean ± *SD*)	Resting State After Fatigue (Mean ± *SD*)	*t*	*p*	Cohen's *d*
LM1	0.260 ± 0.591	−0.002 ± 0.114	2.676	**0.012**	0.46
RM1	−0.062 ± 0.165	−0.022 ± 0.053	−1.481	0.148	0.25
LPM	−0.010 ± 0.121	−0.004 ± 0.033	−0.272	0.788	0.05
RPM	0.016 ± 0.170	−0.002 ± 0.040	0.621	0.539	0.11
LS1	0.017 ± 0.469	0.011 ± 0.127	0.074	0.942	0.01
RS1	0.035 ± 0.159	−0.008 ± 0.043	1.820	0.078	0.31
LDLPFC	0.033 ± 0.114	−0.018 ± 0.047	2.238	**0.032**	0.38
RDLPFC	0.047 ± 0.133	0.001 ± 0.057	2.378	**0.023**	0.41
LVLPFC	0.021 ± 0.079	−0.014 ± 0.036	2.330	**0.026**	0.40
RVLPFC	−0.025 ± 0.249	0.004 ± 0.079	−0.684	0.499	0.12
LFPA	−0.017 ± 0.078	−0.011 ± 0.052	−0.294	0.770	0.05
RFPA	0.014 ± 0.055	−0.015 ± 0.042	2.493	**0.018**	0.43
LOFA	0.012 ± 0.069	−0.018 ± 0.058	2.055	**0.048**	0.35
ROFA	0.021 ± 0.076	−0.018 ± 0.064	2.217	**0.034**	0.38

Bold values in the table indicate brain regions with significant differences and their corresponding *p*-values; $t > 0$ indicates before fatigue > after fatigue, $t < 0$ indicates before fatigue < after fatigue. HbO_2: Oxyhemoglobin; LM1: Left Primary Motor Cortex; RM1: Right Primary Motor Cortex; LPM: Left Premotor and Supplementary Motor Cortex; RPM: Right Premotor and Supplementary Motor Cortex; LS1: Left Primary Somatosensory Cortex; RS1: Right Primary Somatosensory Cortex; LDLPFC: Left Dorsolateral Prefrontal Cortex; RDLPFC: Right Dorsolateral Prefrontal Cortex; LVLPFC: Left Ventrolateral Prefrontal Cortex; RVLPFC: Right Ventrolateral Prefrontal Cortex; LFPA: Left Frontal Pole Area; RFPA: Right Frontal Pole Area; LOFA: Left Orbitofrontal Area; ROFA: Right Orbitofrontal Area.

Table 4
Brain regions with HbO_2 differences before and after lower limb exercise.

Brain region	Resting State Before Fatigue (Mean ± *SD*)	Resting State After Fatigue (Mean ± *SD*)	*t*	*p*	Cohen's *d*
LM1	−0.022 ± 0.321	−0.011 ± 0.068	−0.170	0.867	0.03
RM1	0.014 ± 0.158	−0.002 ± 0.042	0.576	0.570	0.11
LPM	0.054 ± 0.136	−0.012 ± 0.034	2.446	**0.022**	0.48
RPM	0.026 ± 0.104	−0.009 ± 0.029	1.875	0.073	0.37
LS1	−0.058 ± 0.368	−0.006 ± 0.077	−0.716	0.480	0.14
RS1	−0.033 ± 0.177	−0.005 ± 0.032	−0.705	0.487	0.14
LDLPFC	0.023 ± 0.046	−0.008 ± 0.025	3.106	**0.005**	0.61
RDLPFC	0.056 ± 0.159	−0.015 ± 0.022	2.223	**0.036**	0.44
LVLPFC	−0.044 ± 0.200	−0.011 ± 0.035	−0.891	0.381	0.17
RVLPFC	−0.132 ± 0.515	−0.019 ± 0.051	−1.122	0.273	0.22
LFPA	−0.010 ± 0.039	−0.005 ± 0.032	−0.404	0.690	0.08
RFPA	−0.013 ± 0.051	−0.012 ± 0.028	−0.030	0.976	0.01
LOFA	−0.018 ± 0.068	−0.012 ± 0.050	−0.295	0.770	0.06
ROFA	−0.017 ± 0.069	−0.015 ± 0.048	−0.152	0.880	0.03

Bold values in the table indicate brain regions with significant differences and their corresponding *p*-values; $t > 0$ indicates resting state before fatigue > resting state after fatigue, $t < 0$ indicates resting state before fatigue < resting state after fatigue. HbO_2: Oxyhemoglobin; LM1: Left Primary Motor Cortex; RM1: Right Primary Motor Cortex; LPM: Left Premotor and Supplementary Motor Cortex; RPM: Right Premotor and Supplementary Motor Cortex; LS1: Left Primary Somatosensory Cortex; RS1: Right Primary Somatosensory Cortex; LDLPFC: Left Dorsolateral Prefrontal Cortex; RDLPFC: Right Dorsolateral Prefrontal Cortex; LVLPFC: Left Ventrolateral Prefrontal Cortex; RVLPFC: Right Ventrolateral Prefrontal Cortex; LFPA: Left Frontal Pole Area; RFPA: Right Frontal Pole Area; LOFA: Left Orbitofrontal Area; ROFA: Right Orbitofrontal Area.

4.2. Relationship between exercise-induced fatigue and cortical blood oxygen levels

This study found that both upper and lower limb exercise-induced fatigue led to a decrease in brain oxygenation levels, particularly in regions associated with movement, such as the primary motor cortex and prefrontal areas. According to the neurovascular coupling principle, the ratio of HbO_2 to HHb in the capillaries surrounding neurons remains relatively constant during the resting state.[37] When transitioning from rest to an active state, there is an increase in HbO_2 to meet the oxygen demand of neuronal activity. This increase in HbO_2 indicates heightened neuronal excitability.[38,39] In this study, significant reductions in HbO_2 were observed in relevant brain regions following upper limb exercise-induced fatigue. This suggests that neuronal activity diminishes post-fatigue compared to the usual resting state. These findings align with Wu et al., who reported decreased brain activation levels after participants completed incremental load exercises to the point of fatigue.[40] The study also highlighted that changes in activation in the left prefrontal cortex influenced activation changes in bilateral motor areas, emphasizing the prefrontal cortex's critical role in fatigue regulation.[40] According to the cognitive resource theory, increased prefrontal activation during exercise-induced fatigue compensates for performance declines in tasks requiring conscious control.[41–43] When cognitive resources are maximized or depleted,[44] individuals cannot continue tasks or exercise due to limited cognitive capacity.[45] This results in reduced activation in both the prefrontal and motor regions.

4.3. Relationship between exercise-induced fatigue and brain functional connectivity

Following upper limb exercise-induced fatigue, there was a significant decrease in the strength of brain functional connectivity,

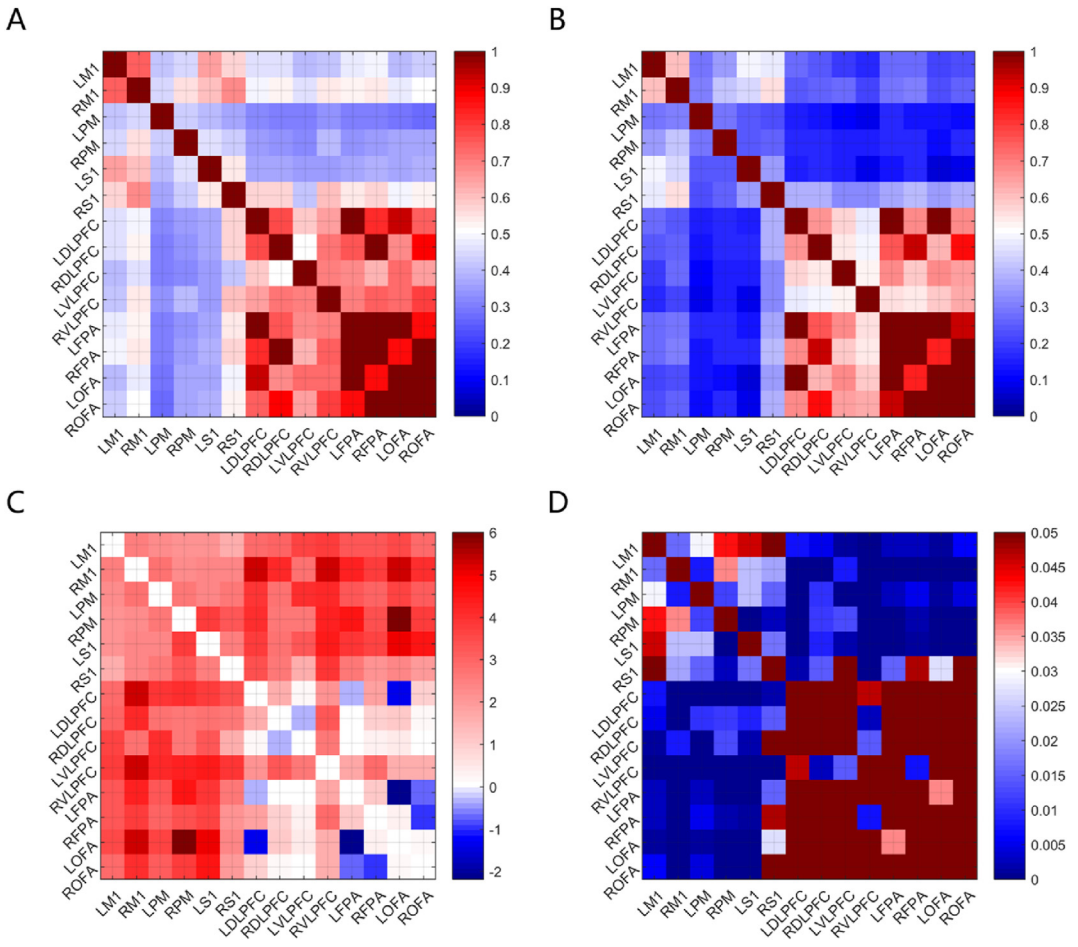

Fig. 4. Interbrain correlation matrix before and after upper limb exercise-induced fatigue. (A) shows the correlation matrix before upper limb motor fatigue, and (B) shows the correlation matrix after upper limb motor fatigue, the redder the color, the stronger the correlation, and the bluer the color, the weaker the correlation. (C) $t > 0$ is shown in red, indicating before fatigue > after fatigue; $t < 0$ is shown in blue, indicating before fatigue < after fatigue. (D)significant differences that pass FDR correction are shown in blue. LM1: Left Primary Motor Cortex; RM1: Right Primary Motor Cortex; LPM: Left Premotor and Supplementary Motor Cortex; RPM: Right Premotor and Supplementary Motor Cortex; LS1: Left Primary Somatosensory Cortex; RS1: Right Primary Somatosensory Cortex; LDLPFC: Left Dorsolateral Prefrontal Cortex; RDLPFC: Right Dorsolateral Prefrontal Cortex; LVLPFC: Left Ventrolateral Prefrontal Cortex; RVLPFC: Right Ventrolateral Prefrontal Cortex; LFPA: Left Frontal Pole Area; RFPA: Right Frontal Pole Area; LOFA: Left Orbitofrontal Area; ROFA: Right Orbitofrontal Area.

particularly within the sensorimotor network (primary motor cortex, premotor, and supplementary motor areas). This result aligns with previous studies that observed weakened functional connectivity between bilateral motor cortices during the resting state after arm muscle fatigue.[46] Additionally, this study noted a reduction in connectivity between the motor cortex and primary somatosensory cortex as well as various prefrontal areas. Research using functional magnetic resonance imaging (fMRI) to explore fatigue progression during finger grip exercises found that with increased fatigue, there was enhanced functional connectivity between the primary motor cortex, premotor cortex, supplementary motor area, primary somatosensory cortex, and prefrontal cortex.[47] This may be due to the changes in motor commands related to fatigue being regulated by the prefrontal cortex, which is responsible for action planning, rhythm strategies, and decision-making.[46] The motor cortex and downstream efferent neural structures directly control movement.[48] In incremental load exercises, fatigue impacts not only the cortical responses associated with information execution and feedback processing but also the resting-state connectivity between different cortical regions.[49] Changes in functional connectivity within the brain's neural network during fatigue reflect the brain's regulation and adaptation mechanisms in response to fatigue. Previous studies have shown that unilateral upper limb fatigue can decrease proprioceptive performance in both upper limbs, indicating that fatigue's impact on brain network connectivity persists beyond the completion of the exercise task.[50] Athletes who performed upper limb cycling and then a 4-km lower limb cycling showed decreased performance in the lower limb task[51] Therefore, it is reasonable to speculate that the reduced brain connectivity following upper limb exercise-induced fatigue could be responsible for the decreased performance in subsequent upper limb tasks. The decline in the connectivity strength within the sensorimotor network likely affects the coordination of motor planning and execution, leading to diminished performance.

Following lower limb exercise-induced fatigue, changes in brain functional connectivity were not significant. The differences in connection strength observed in the *t*-value map were relatively balanced between enhancements and reductions, indicating that brain regions maintained relatively stable connectivity even in a fatigued state. Before correction, some areas showed increased connectivity strength, such as between the left dorsolateral prefrontal cortex and the left orbitofrontal cortex, and between the left orbitofrontal cortex and bilateral frontal poles. This contrasts with the results observed after upper limb fatigue.[35] One possible reason for this observation is the difference in exercise characteristics. Lower limb exercises and upper limb exercises engage different muscle groups and involve different movement patterns. Lower limb cycling involves larger muscle groups and tends to be more holistic and sustained, whereas upper limb exercises are often more localized and shorter in duration. This distinction may lead to different brain responses to lower limb exercise-induced fatigue.

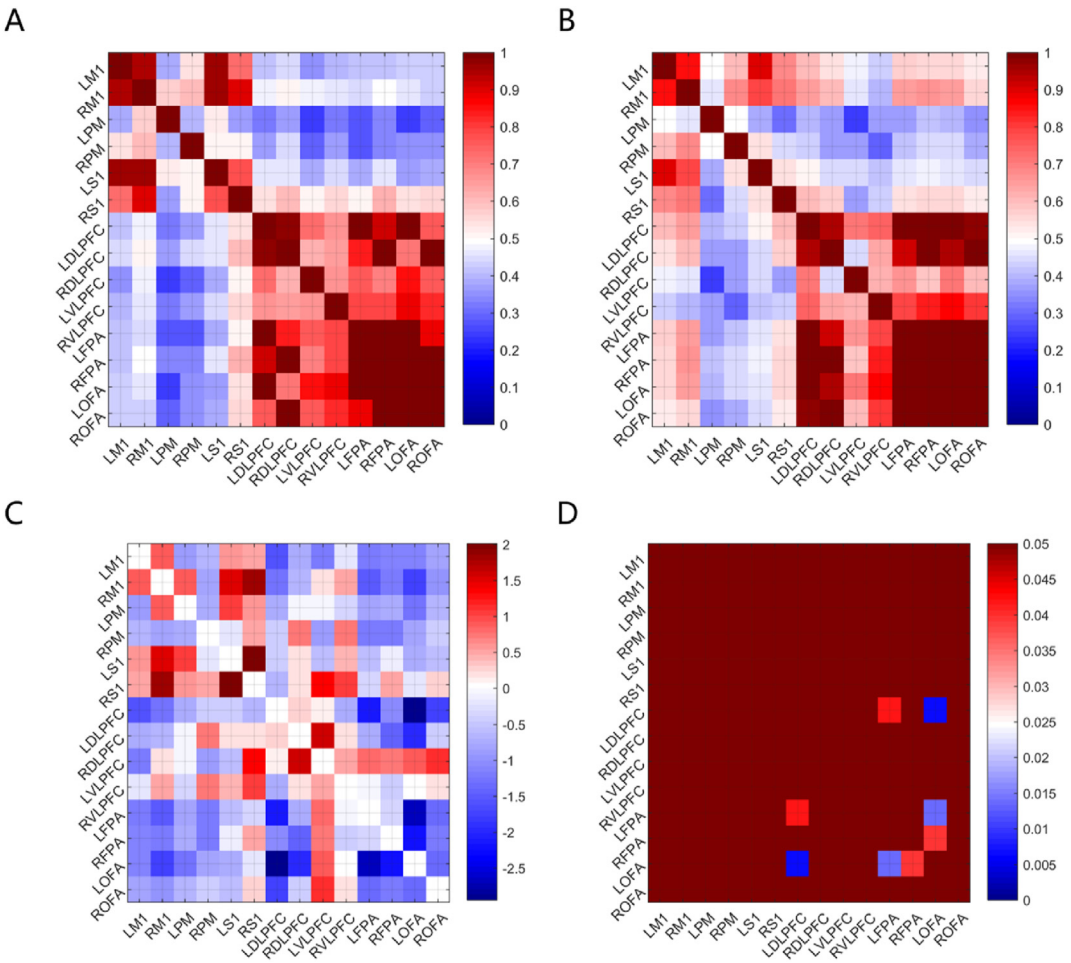

Fig. 5. Interbrain correlation matrix before and after lower limb exercise-induced fatigue. (A) shows the correlation matrix before lower limb motor fatigue, and (B) shows the correlation matrix after lower limb motor fatigue, the redder the color, the stronger the correlation, and the bluer the color, the weaker the correlation. (C) $t > 0$ is shown in red, indicating before fatigue > after fatigue; $t < 0$ is shown in blue, indicating before fatigue < after fatigue. (D) significant differences ($p < 0.05$) are shown in blue, but they did not pass FDR correction. LM1: Left Primary Motor Cortex; RM1: Right Primary Motor Cortex; LPM: Left Premotor and Supplementary Motor Cortex; RPM: Right Premotor and Supplementary Motor Cortex; LS1: Left Primary Somatosensory Cortex; RS1: Right Primary Somatosensory Cortex; LDLPFC: Left Dorsolateral Prefrontal Cortex; RDLPFC: Right Dorsolateral Prefrontal Cortex; LVLPFC: Left Ventrolateral Prefrontal Cortex; RVLPFC: Right Ventrolateral Prefrontal Cortex; LFPA: Left Frontal Pole Area; RFPA: Right Frontal Pole Area; LOFA: Left Orbitofrontal Area; ROFA: Right Orbitofrontal Area.

4.4. Limitations

Firstly, previous studies have suggested that resting-state cortical connectivity can serve as an indicator of fatigue recovery.[46] However, this study only measured the immediate post-exercise brain oxygenation levels of participants, which does not allow for the assessment of brain activity and network characteristics during the fatigue recovery process. Secondly, the study did not measure cognitive or behavioral performance before and after fatigue. The impact of the observed changes in network connectivity on cognitive or behavioral performance needs further investigation. Lastly, this study used an incremental load exercise protocol, which does not separate the effects of time from the effects of intensity.[41] Future research should consider exploring the impact of exercise duration and intensity on brain activity and network connectivity in more detail.

5. Conclusion

The results of this study indicate that both upper limb and lower limb exercise-induced fatigue lead to significant decreases in cortical oxygenation levels. However, upper limb exercise-induced fatigue results in a significant reduction in cortical functional connectivity strength, whereas changes in connectivity after lower limb exercise-induced fatigue are not significant. This suggests that the brain employs different regulatory mechanisms in response to different forms of exercise-induced fatigue. Future research should focus on the relationship between cortical changes induced by exercise-induced fatigue and performance-related metrics to better understand the impact of fatigue.

CRediT authorship contribution statement

Feng Li: Writing – original draft, Supervision, Methodology, Data curation, Conceptualization. **Yajie Wang:** Writing – review & editing, Investigation, Data curation. **Xinyi Wang:** Writing – review & editing, Investigation, Data curation. **Jiawei Bi:** Writing – review & editing, Supervision, Methodology. **Ye Luo:** Writing – review & editing, Methodology, Investigation, Data curation. **Lingyan Huang:** Writing – review & editing, Supervision, Project administration.

Ethical approval statement

Written informed consent was obtained from all the participants prior to data collection. This study was reviewed and approved by the Ethics Committee of Shanghai University of Sport in accordance with the Declaration of Helsinki (NO.102772023RT031).

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Declaration of competing interest

There are no conflicts of interest to declare. Each of the authors has read and concurs with the content in the final manuscript.

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