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Exercise, nutrition, and cognitive function: Implications on health promotion and performance improvement

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Published in
Frontiers in Human Neuroscience

ISSN 1664-8714
ISBN 978-2-8325-2327-8
DOI 10.3389/978-2-8325-2327-8

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Exercise, nutrition, and cognitive function: Implications on health promotion and performance improvement

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Citation
Huang, J., Hu, M., Sun, F., Wei, G.-X., Yuan, T.-F., Cooper, S. B., eds. (2023). *Exercise, nutrition, and cognitive function: Implications on health promotion and performance improvement*. Lausanne: Frontiers Media SA.
doi: 10.3389/978-2-8325-2327-8

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frontiers | Frontiers in Human Neuroscience

TYPE Editorial
PUBLISHED 18 April 2023
DOI 10.3389/fnhum.2023.1190188

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OPEN ACCESS

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RECEIVED 20 March 2023
ACCEPTED 31 March 2023
PUBLISHED 18 April 2023

CITATION
Sun F, Huang J, Hu M, Wei G, Yuan T and Cooper SB (2023) Editorial: Exercise, nutrition, and cognitive function: implications on health promotion and performance improvement. *Front. Hum. Neurosci.* 17:1190188. doi: 10.3389/fnhum.2023.1190188

Editorial: Exercise, nutrition, and cognitive function: implications on health promotion and performance improvement

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KEYWORDS

exercise, nutrition, cognitive function, health promotion, performance improvement

Editorial on the Research Topic
Exercise, nutrition, and cognitive function: implications on health promotion and performance improvement

Cognitive function defines performance in objective tasks (e.g., memory, attention, and executive function) that require conscious mental effort (Taylor et al., 2016). The decreased cognitive function has been suggested to be associated with the development of comorbid diseases, increased risk of dementia and related neurodegenerative diseases, and been considered a marker of preclinical disease (Campbell et al., 2013). In recent years, efforts have been made in investigating the lifestyle factors which may ameliorate cognitive functions. Physical activity and exercise have been suggested to be a modifiable lifestyle factor to maintain or improve cognitive function, prevent cognitive decline, and/or the development of several neurodegenerative diseases (Jia et al., 2019; Mahalakshmi et al., 2020). However, it is still unclear what kind of exercise may affect cognitive function more significantly. More studies are still needed to investigate the optimal exercise mode, exercise intensity, and exercise frequency, as well as explore the potential mechanisms behind the changes in cognitive function.

In this Research Topic, a total of 10 papers were published to cover the above-mentioned aspects among different populations.

One cross-sectional study (Liu et al.) examined the association between gross motor skills and inhibitory control in 123 preschool children, and the results indicated a significant negative correlation between gross motor skills and the reaction time of inhibitory control. Another cross-sectional study (Cui et al.) recruited 700 Chinese adolescents and investigated the associations between specific-type sedentary behaviors (i.e., screen-based and educational) and cognitive flexibility. It was found that recreational screen-based sedentary time was negatively correlated with cognitive flexibility, whereas educational sedentary time was positively correlated with cognitive flexibility. These two studies further suggested the close relationship between movement behaviors and cognitive functions among youth. For the elderly, another study (Yu et al.) investigated the effects of two different exercise interventions, i.e., Tai Chi and Brisk Walking, on cognitive function among individuals aged 60 and greater. Although the sample size is relatively small ($n = 21$ in Tai Chi group and $n = 22$ in Brisk Walking group), the results suggested that both exercise interventions improved general cognitive performance. However, it seems that Tai Chi group has resulted a better memory performance than Brisk Walking group.

Besides the general population, one study (Malcolm et al.) investigated the effects of a competitive hockey sports match on cognitive function in a randomized crossover design. Compared with the control trial (i.e., seated rest), the match improved the performances of perception and complex executive function tasks whereas decreased the working memory performance. It is worth noting that several hormones and neurotransmitters were also measured in this specific study to explore the potential mechanisms. Another study (Wang, Chen et al.) adopted the bibliometric methods and the visual analysis methods to analyze 885 studies of physical activity intervention in autism spectrum disorder (ASD) population. The results suggested that physical activity can improve ASD symptoms, especially in children and adolescents with ASD. Obviously, the literature in this area showed a growing trend. The authors have suggested two potential research directions, i.e., the long-term effects of physical activity interventions on ASD and the sustainability of benefits of different physical activity interventions. A multidimensional exercise-integrated intervention model may be necessary to be constructed.

Besides the original studies, two systematic review papers were also published in this Research Topic. One paper (Wen et al.) summarized the effects of whole-body vibration training on cognitive functions. The majority of included studies in this review suggested that whole-body vibration training may be a useful strategy for the management of cognitive impairment. However, more studies are needed to verify this conclusion. Another review paper (Wu et al.) tried to explore the neuronal effects of exercise on inhibitory control functions. With 14 included fMRI studies and 397 participants, the results suggested that the effect of exercise on neural activity is related to inhibitory control in the extended frontoparietal, default mode network, visual network, and other pathways.

One included study in this Research Topic (Wang, Zhu et al.) first investigated the effects of different types of fatigue-recovery breaks on the cognitive processes by evaluating the corresponding behavioral improvement and neural response in a sustained attention task, i.e., a continuous 30-min psychomotor vigilance tasks. It was observed that both the mid-task cycling and mid-task rest could restore objective vigilance transiently, while subjective feeling was only maintained after mid-task rest. The divergent patterns of EEG change were observed during post-break improvement.

With the adaptation of fMRI, another study (Shi et al.) recruited 99 healthy adults and examined whether mind wandering modulated the relations between physical activity and resting-state hippocampal functional connectivity. The results indicated that mind wandering was negatively related to the resting-state functional connectivity between the hippocampus and the right inferior occipital gyrus. However, for participants with different levels of mind wandering, the relationships between physical activity and resting-state functional connectivity are different. The authors suggested that individual differences should be considered when promoting physical activity to maintain or improve cognitive functions.

The last paper in this Research Topic (Li et al.) investigated behavioral and neural responses to drug-related stimuli using a self-report scale, and a cued-action task in conjunction with EEG among a group of 52 methamphetamine addicts. The results suggested that increased attentional resources were allocated to the processing of drug-related stimuli and the pathways responsible partially overlap with those recruited in processing positive emotional imagery in addicts.

In summary, there are large varieties among the included studies in this Research Topic. However, most of the studies further support the benefits of physical activity on cognitive functions among different populations. More importantly, different measurements such as brain image, EEG, and blood neurotransmitters, have been adopted to explore the potential mechanisms. Additionally, nutrition is another important factor that may affect cognitive functions (Spencer et al., 2017; Gutierrez et al., 2021). So far, the combined effects of different exercise protocols and nutritional strategies on cognitive function are still unclear. Unfortunately, no related studies were included in this Research Topic. Obviously, more studies are still needed in this interesting and important research area.

Author contributions

JH wrote the introduction and the conclusion. FS wrote the central part with comments on the cited papers and references. All authors contributed to the article and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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frontiers in Human Neuroscience

ORIGINAL RESEARCH
published: 04 March 2022
doi: 10.3389/fnhum.2022.829924

The Influence of a Competitive Field Hockey Match on Cognitive Function

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Despite the known positive effects of acute exercise on cognition, the effects of a competitive team sport match are unknown. In a randomized crossover design, 20 female and 17 male field hockey players (19.7 ± 1.2 years) completed a battery of cognitive tests (Visual Search, Stroop, Corsi Blocks, and Rapid Visual Information Processing) prior to, at half-time, and immediately following a competitive match (or control trial of seated rest); with effect sizes (ES) presented as raw ES from mixed effect models. Blood samples were collected prior to and following the match and control trial, and analyzed for adrenaline, noradrenaline, brain derived neurotrophic factor (BDNF), cathepsin B, and cortisol. The match improved response times for a simple perception task at full-time (ES = –14 ms; $P < 0.01$) and response times on the complex executive function task improved at half-time (ES = –44 ms; $P < 0.01$). Working memory declined at full-time on the match (ES = –0.6 blocks; $P < 0.01$). The change in working memory was negatively correlated with increases in cortisol ($r = -0.314$, $P = 0.01$; medium), as was the change in simple perception response time and the change in noradrenaline concentration ($r = -0.284$, $P = 0.01$; small to medium). This study is the first to highlight the effects a competitive hockey match can have on cognition. These findings have implications for performance optimization, as understanding the influence on specific cognitive domains across a match allows for the investigation into strategies to improve these aspects.

Keywords: perception, executive function, BDNF, neurobiological changes, catecholamines

OPEN ACCESS

Edited by:
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Specialty section:
This article was submitted to Cognitive Neuroscience, a section of the journal Frontiers in Human Neuroscience

Received: *06 December 2021*
Accepted: *20 January 2022*
Published: *04 March 2022*

Citation:
Malcolm R, Cooper S, Folland JP, Tyler CJ and Sunderland C (2022) The Influence of a Competitive Field Hockey Match on Cognitive Function. Front. Hum. Neurosci. 16:829924. doi: 10.3389/fnhum.2022.829924

INTRODUCTION

In open skill sports such as field hockey, skill is determined by a player's ability to adapt and perform a specific action despite the environmental constraints imposed upon them by calling upon neural resources from changeable regions of the brain (Allard and Burnett, 1987; Starkes, 1987; Williams and Jackson, 2019; Morris-Binelli et al., 2020). With the recently adapted rules, field hockey has become one of the most fast paced team sports, hence the ability to anticipate, adapt and respond successfully relies on superior perceptual-cognitive factors (Morris-Binelli et al., 2020). Williams and Jackson (2019) highlight the many different perceptual cognitive skills that contribute to team sports performance, including the ability to scan, using visual processes, in a more efficient manner in order to extract relevant cues. These authors emphasize that understanding the influence of a match on specific perceptual cognitive skills would significantly enhance team performance. Cognition, encompassing visual perception, executive function, sustained attention and working memory, influences many aspects of skill performance in team sports; however, an important component is likely due to the influence of the prefrontal cortex in monitoring errors made and shifting neural resources accordingly to positively influence responses (Arnsten, 2009). Therefore, athletes who can anticipate necessary responses successfully, overcoming the spatio-temporal constraints, are likely to be superior team sports athletes (Williams and Jackson, 2019).

Although cognitive function is often discussed as an overall phenomenon, it consists of a number of sub-components such as perception, memory, attention and executive function (Schmitt et al., 2005); all of which contribute to successful skill, and sporting, performance. A number of examples span across these domains, including the ability to recognize and recall patterns within a match, the ability to evaluate and prioritize the importance of unfolding events and using perception to scan and react efficiently to cues (Williams and Jackson, 2019). Therefore, it is important to understand the effect of team sport exercise across a range of domains of cognition. Bandelow et al. (2010) used a variety of cognitive tests, all of which had relevance to team sports players. A visual search test was used which allows for the analysis of visual perception. In a hockey specific example, perception has been highlighted (using interviews) as a key factor in goalkeeper's abilities to successfully save penalty corner attempts (Morris-Binelli et al., 2020). Cañal-Bruland et al. (2010) assessed this using a laptop simulation of penalty corners and found visual search strategies, where gaze is shifted to the location of the ball-and-stick, enabled improved performance in the goal keepers. These findings can be applied to outfield players who are required to react to the position of the ball or opposing players in order to select the correct action. Although this research provides an insight into how cognition influences skill performance, the research assessing how the physical load, in combination with cognitive load, of sport influences cognition remains limited (Schapschröer et al., 2016). The review by Schapschröer et al. (2016) found that the impact of exercise on skill performance was influenced by the specificity of the exercise, as well as the cognitive task, with expert athletes demonstrating a positive response in speed of reaction but no change in accuracy. Hence understanding how an athlete's cognition, across a range of domains, varies across a competitive match, will help to understand the perceptual-cognitive relationship.

The influence of exercise on executive function has also been extensively researched in laboratory-based studies (Schmit and Brisswalter, 2020). This domain is particularly important in team sports players as executive function assesses how players adaptively respond to novel stimuli and develop new strategies in order to respond accurately and effectively. Working memory, a sub domain of executive function, enables the assessment of how well a player can retrieve information from both immediate experiences, e.g., a previous interaction on the pitch, and longer term experiences, e.g., tactical information provided prior to the match (Strauss et al., 2006). Finally, sustained attention plays a role across all domains, through the ability the be able to perform skills throughout a match, despite increased mental and physical fatigue (Hajar et al., 2019). However, in order to understand how to enhance these aspects of cognition during team sport performance, it is important to understand (a) the effect of a competitive team sport match across a range of domains of cognition, and (b) the potential physiological variables responsible for these effects.

Heightened arousal, via increased secretion of catecholamines (adrenaline and noradrenaline), has consistently been named as a contributor to exercise-induced cognitive changes (McMorris and Graydon, 1997). The influence of catecholamines on cognition has traditionally followed an inverted-U relationship, whereby cognition improves up to a certain point, alongside increases in catecholamines, until over arousal began to have a negative effect on the prefrontal cortex, and resulting cognition (Arnsten, 2009). However, the inverted-U has received some criticism in recent years, with Schmit and Brisswalter (2020) suggesting the relationship is far more complex and dynamic than first assumed.

Brain-derived neurotrophic factor (BDNF) has been investigated in response to both acute and chronic exercise protocols (Winter et al., 2007; Griffin et al., 2011). Winter et al. (2007) found that increased BDNF concentration was increased following high impact anaerobic sprint intense exercise, an effect that was related to a 20% improvement in short-term learning, however, the effect in team sports is still unknown. Cathepsin B (a muscle secretory factor that is increased post-exercise) has also recently been recognized to contribute to the positive memory alterations in response to treadmill exercise (Moon et al., 2016). Contrastingly high levels of cortisol, a hormone released in response to stress (McMorris et al., 2006), have been found to detrimentally influence cognition (Kirschbaum et al., 1996). This effect is via the action of glucocorticoid receptors in the prefrontal cortex (Oei et al., 2006), resulting in the blocking of catecholamine transporters (Arnsten, 2009). Therefore, emerging evidence suggests that a number of different blood parameters (e.g., catecholamines, cathepsin B, BDNF, cortisol) can contribute to enhancing our understanding of the exercise-cognition relationship, yet the impact of team sports on cognition and blood parameters are yet to be examined together.

Cognitive function is also known to be sensitive to perceptual changes and changes in mood (Malcolm et al., 2018), two aspects which are likely to fluctuate across a team sports match. Hence, considering the range of factors that influence cognition (neurohormones, mood, and affect) is essential to a better understanding of this relationship.

Studies have tried to mimic the demands of match-play in a laboratory to investigate the influence of intermittent team sport activity on skill performance in soccer (McGregor et al., 1999) and, hockey (Sunderland and Nevill, 2005). These laboratory assessments provide us with an understanding of how high intensity intermittent exercise influences cognition; however, in order to truly understand the impact of team sport itself, an ecologically valid field-based assessment is required. To our knowledge, the only study to address this area to date assessed the influence of a field-based competitive football match on cognitive function Bandelow et al. (2010). However, this study was performed at high external temperatures (∼34°C), which presents a confounding variable due to the known effects of heat on cognition (Gaoua et al., 2011; Liu et al., 2013; Malcolm et al., 2018). Consequently, due to the challenges around collecting data in a match context, there is no study that has assessed the influence of an intermittent team sport match on cognitive function in a temperate environment, despite the importance of understanding this to facilitate the optimization of skill performance.

Therefore, the aim of the current study was to establish the influence of a competitive field hockey match on cognitive performance (perception, working memory, executive function); and to examine changes in blood parameters and mood as potential explanatory variables for these effects. It is hypothesized that response times will improve for perception and executive function tasks, with a trade-off occurring with accuracy, while the remaining cognitive tasks will be unaffected by the competitive exercise stress.

MATERIALS AND METHODS

Twenty female athletes (mean ± SD: age 19.6 ± 1.1 years, height 1.67 ± 0.03 m, body mass 64.7 ± 6.3 kg) and seventeen male athletes (age 19.8 ± 1.3 years, height 1.83 ± 0.07 m, body mass 77.9 ± 6.3 kg) volunteered for the study. The participants were recruited due to their affiliation with a hockey club and played for one of four teams across the club at an elite (7 training sessions and 2 matches per week) or sub-elite level (4 training sessions and 2 matches per week), and across all outfield positions. Ethics was gained from the institution's invasive ethical advisory committee prior to data collection (approval code 403). All participants were provided with an information sheet and completed an informed consent form and health screen questionnaire prior to participation.

Study Design

This study was a randomized, order-balanced, crossover design, whereby participants all completed one familiarization session (at least 1 week prior to their first main trial), one match trial and one rested control trial. Data collection across the 4 teams was between September and March. The study was order balanced by half the participants completing the control trial the day before the match, and half completing the trial the day after. Participants completed a 24 h food diary prior to the first main trial and replicated prior to the second main trial. The average temperature across the 8 trial days (control and match) was 10.3 ± 2.7°C.

Familiarization

Height was measured using a stadiometer (Seca 123, Seca Ltd.) to the nearest 0.1 cm and nude body mass was measured to the nearest 0.1 kg (GFK 150 AEADAM digital scale, Vitech scientific Ltd.). The participants completed a full battery of the cognitive function tests [visual search, stroop test, corsi blocks and rapid visual information processing (RVIP)] to familiarize themselves with the tests, as completed in previous research (Malcolm et al., 2018).

Protocol

Data were collected during four competitive field hockey matches and simulated control days. The participants arrived 2 h prior to the start of the match or control trial, and 2 h post-prandial. A urine sample was taken on arrival to measure urine osmolality (Osmocheck, Pocket PAL-OSMO, Japan). The participants who were deemed hypohydrated (urine osmolality > 800 mosmol.kg^{-1}) were instructed to drink 0.5 L of water and re-tested in 30 min, until urine osmolality was < 800 mosmol.kg^{-1}. This was completed due to the known impact of hypohydration on cognition (Judelson et al., 2007). Nude body mass was then collected in privacy, to the nearest 0.1 kg (GFK 150 AEADAM digital scale, Vitech scientific Ltd.). This was repeated following the completion of each trial (**Figure 1**). The change in body mass was then corrected for urine output and fluid intake to determine sweat loss and estimate hydration status.

On match day trials, the participants were fitted with a global positioning system unit (GPS) (SPI Pro, GPSports, Fyshwick, Australia) and heart rate monitor (Polar Electro, Kemple, Finland), whereas only heart rate monitors were worn on the control trials. Cognitive data was collected at three time points, relative to the timings of the match (1 h pre-match, at half time (shortened testing battery) and immediately post-match), where half time occurred after 35 min and full time following 70 min of match play. Cognitive tests were conducted in a private room immediately next to the hockey pitch. Lights were turned off, windows covered and noise canceling headphones worn to ensure no distracting stimuli occurred. All participants left the pitch immediately following the half-time and final whistle, beginning the tests within 2 min. All matches were league matches and took place in Loughborough, England between September 2015 and March 2016. The temperature and humidity were not different between control and match trials for all participants ($P > 0.05$). All timings and measurements were the same on the control trial, with the exception of the warm-up and match, which were replaced by seated rest. The participants were allowed to converse and read during the control trial rest periods, but no cognitively challenging or demanding activities were permitted.

The participants were instructed to eat as normal until 2 h prior to arrival for main trials and then not permitted to eat until the trial was completed. Water was consumed *ad libitum* during both trials (and measured), and the participants were encouraged to drink frequently during the 24 h leading to the trial to ensure euhydration. The participants were asked to avoid caffeine on the day of each trial, and avoid alcohol and exercise in the 24 h prior to each trial. The participants completed a 24 h food diary prior to their first main trial and were asked to repeat this prior to their subsequent trial in order to minimize metabolic fluctuations.

Measurements

Cognitive Function Tests

A battery of cognitive function tests (visual search test, Stroop test, Corsi blocks and RVIP) was administered using a laptop computer (Thinkpad T450, Lenovo PC HK Limited, China) 1 h prior to and immediately following the competitive field hockey match. Each participant had their own laptop for the duration of the study, allowing a full team to complete their cognitive tests at the same time. Tests were always completed in the order

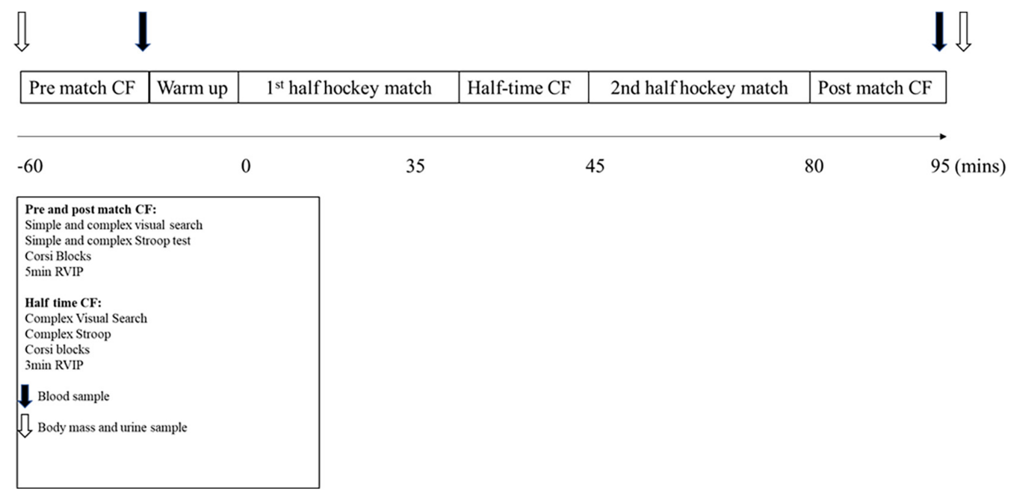

FIGURE 1 | Schematic of the match day protocol. CF, Cognitive function; RVIP, rapid visual information processing. Data is mean ± SD.

stated above. The full version of the cognitive battery consisted of a simple and complex visual search test, a simple and complex Stroop test, Corsi blocks test and 5 min RVIP test. A shortened version of the battery of tests was administered at half time due to the time constraints, including the complex level of the visual search and Stroop tests, the Corsi blocks test and 3 min of the RVIP test. The full battery lasted ∼ 14 min and the shortened battery ∼ 7 min. Participants sat at individual desks, spaced around the room and wore noise-canceling headphones to eradicate any distracting stimuli. Prior to each test (and test level), 3–6 practice stimuli were presented to re-familiarize participants with the task and eradicate any learning effect.

Perception (Visual Search Test)

Perception and visual processing were assessed using the Visual Search test, as used by Cooper et al. (2015). The test is made up of two levels, with 21 stimuli on each. On the simple level of this test participants were required to react as quickly as possible to the presence of a bold, solidly outlined, green triangle. The complex level of the test required participants to complete the same task, however, the triangle shape was made up of several dots. The background was covered in green dots, which were redrawn every 250 ms, with the aim of inducing the visual effect of a flickering background. For both levels of the test the location and intervals of appearance of the stimuli, was randomized. Participants were instructed to respond to the stimuli as quickly as possible, by pressing the space bar. In order to assess visual processing and perception, this test scrutinizes the capacity to focus on specific cues whilst ignoring distracting information. The response time of correct responses and the proportion of the correct responses achieved were both measured, for each level of the test.

Executive Function (Stroop Test)

In order to assess executive function and selective attention, both controlled by frontal lobe function, the Stroop test was administered (Stroop, 1935). The test is comprised of two levels. The aim of the test is to assess the ability to suppress an automated response hence each level has varying amounts of interference to regulate the level of difficulty. Each level involves a test word appearing in the center of the screen, with a target word and a distractor either side of it. The target word's position was counterbalanced for the left and right side within each test level. The participant was instructed to select the target word's position, using the right and left arrow key, as quickly as possible once the words appeared on the screen.

Twenty stimuli were used for the simple level of the test and 40 stimuli for the complex level. On the simple level of the Stroop test, all words were presented in white font and the participant was instructed to select the word which matched the target word in the center of the screen. The color interference complex level of the test required the participant to select the word which matches with the color the word in the center of the screen was written in, rather than the word itself (which was an incongruent color). The choices stayed on the screen until the participant made a response. Following the response, an inter-stimulus interval of 1 s took place, prior to the next selection of stimuli appearing. The main outcome measures were the response time of correct responses and the proportion of correct responses.

Working Memory (Corsi Blocks)

Visuo-spatial short-term working memory is measured using the Corsi Blocks test (Corsi, 1972). Squares within a 3 × 3 grid are lit up in a random order. Participants are required to click on the boxes on the screen, in the order in which they lit up. Initially, three boxes are lit up in a sequence, thereafter, after each correctly remembered sequence, one additional box is lit up. If participants reached a sequence length of 9 correctly remembered boxes, the grid increased in size to 4 × 4. Performance was determined by the mean of the 3 longest correctly remembered sequences (Cooper et al., 2016).

Attention (Rapid Visual Information Processing)

Sustained attention is measured using the RVIP, as implemented by Hogervorst et al. (2008). The test lasted 5 min, during which the numbers between 2 and 9 appeared on the screen at 600 ms intervals. The participants were instructed to press the space bar as quickly as possible whenever detect target sequences of three consecutive odd or even numbers (e.g., "2-8-4," "9,5,3") appeared on the screen. There were 8 target sequences per min. For each target sequence, the participants could only respond during or within the 1,500 ms immediately following the sequence. The outcome measures were the response time of correct responses and the proportion of correct responses made.

Global Positioning System Unit

For the duration of the match, players wore a GPS monitor (GPS, GPSports Ltd.), mounted between the shoulder blades. GPS transmitters assessed total distance ran. Distances covered were split into 6 different speed zones; 0–4 $km.h^{-1}$, 4–7 $km.h^{-1}$, 7–11 $km.h^{-1}$, 11–15.5 $km.h^{-1}$, 15.5–20 $km.h^{-1}$, > 20 $km.h^{-1}$. Time spent off the pitch (e.g., during substitutions or following sending off) was not included. Data were analyzed using GPSports team AMS v.1.2.1.11.

Heart Rate

Heart rate monitor belts (Polar Electro Team Sport System, Kemple, Finland) were worn throughout both main trials, to provide heart rate data every 5 s.

Mood Questionnaire

A shortened version of the Brunel Mood Scale (BRUMS) questionnaire (Terry et al., 1999) was completed by the participants immediately prior to the first and final battery of cognitive function tests (pre-match and full-time). The participants answered 24 items linked to 6 aspects of mood; anger, confusion, depression, fatigue, tension and vigor. Each of these items was ranked on a scale of 1–5 (where 1: "not at all," 2: "a little," 3: "moderately," 4: "quite a lot," 5: "extremely"), this generated a total out of 20 for each facet of mood, which was used for analysis.

Blood Analyses

Due to issues with blood sample collection, not all data sets are complete. The sample size for each marker is reflected in the results. Blood samples were taken immediately following pre-match and post-match cognitive function testing, via venepuncture. This was completed within 2 min of completing the cognitive test battery, and blood was immediately treated. For serum samples, approximately 5 ml of blood was pipetted into an anticoagulant-free tube (Sarstedt, Germany) and allowed to clot for 30 min. Following this the sample was centrifuged (accuSpin 1R centrifuge, Fisher Scientific, Germany) for 10 min at 3,000 g. For plasma samples, 5 ml of blood was pipetted into each of two lithium heparin tubes (Sarstedt, Germany). Tubes were inverted five times and immediately centrifuged (accuSpin 1R, Fisher Scientific, Germany) for 10 min at 3,000 g. The supernatant for both plasma and serum was removed using a pipette, dispensed into eppendorfs and initially frozen at −20°C and then at −80°C until analyses were performed. Due to the short half-life of catecholamines, a single plasma eppendorf was snap frozen for the analysis of adrenaline and noradrenaline. Plasma was also analyzed for Cathepsin B and estrogen (female participants). Serum was analyzed for cortisol and BDNF.

All blood analysis and intra-assay CV analysis was completed by the lead researcher. Plasma was analyzed for adrenaline (*intra-assay CV: 10.5%*) and noradrenaline (*intra-assay CV: 6.5%*) using manual enzyme immunoassay (CatCombi ELISA, IBL International GmbH, Hamburg, Germany) and for Cathepsin B (*intra-assay CV: 7.6%*) via ELISA (Cathepsin B Human ELISA Kit, Abcam, Cambridge, United Kingdom). Serum was analyzed for cortisol (*intra-assay CV: 12.4%*) using an immunoassay (Cortisol, R&D systems, Abingdon, United Kingdom) and for BDNF (*intra-assay CV: 12.1%*) using separate immunoassay procedures (Human Free BDNF, R&D systems, Abingdon, United Kingdom). A 20-fold dilution was used for both cortisol and BDNF. For female participants, baseline plasma samples on the control and match day were analyzed for estrogen (estrogen, R & D systems, Abingdon, United Kingdom) in order to identify any changes in the stage of the menstrual cycle between trials.

Data Analysis

Physiological data and corsi blocks data were analyzed using SPSS (Version 23, SPSS Inc., Chicago, Il, United States) via two-way repeated measures Analysis of Variance (ANOVA), using a trial by time approach. Where paired comparisons were required, paired samples *t*-tests with Bonferroni corrections were conducted.

The remaining cognitive data (Stroop, visual search and RVIP) were analyzed using mixed effect models in R.[1] Response time analyses were performed using the *nlme* package (yielding *t* statistics) and accuracy analyses were performed using the *lme4* package (yielding *z* statistics), to account for the binomial nature of accuracy data. Due to the shortened battery of tests at half-time, two analyses were run. The first analysis assessed changes from pre-match to half time, and the second analysis assessed changes from pre-match to full-time. For cognitive variables, effect sizes (ES) are reported as raw effect sizes from the mixed effect models, demonstrating the magnitude of the interaction effect. Effect sizes are reported relative to the control trial (i.e., a negative effect size for response times indicates a greater improvement in response times on the match trial, a positive effect size for accuracy indicates an improvement in accuracy on the match trial). The effect size (Cohen's d) of mood and blood parameters were calculated using *post hoc* pairings using the following thresholds: < 0.2 = trivial effect; 0.2- < 0.5 = small effect; 0.5–0.8 = moderate effect and > 0.8 = largest effect.

Pearson's correlation coefficients were computed for correlations between absolute change in blood parameters (adrenaline, noradrenaline, BDNF, cathepsin B and cortisol) and absolute change in cognitive task performance. Correlations were also run between changes in blood parameters and match variables (e.g., GPS data). There were also run alongside change in cognitive task performance. A positive relationship will signify both variables increasing or decreasing, vs. a negative relationship where one variable increases, while the other decreases. The larger the absolute value of the correlation

[1] www.r-project.org

TABLE 1 | Cognitive function data across the control and match day trials.

Test	Variable	Test level	Control			Match			Trial effect	Time effect	Interaction
			Pre	HT	FT	Pre	HT	FT			
Visual search	Response time (ms)	Simple	284 ± 24		302 ± 41	293 ± 25^		298 ± 32^&+	$P < 0.01$	$P < 0.01$	$P < 0.01$
		Complex	1,114 ± 190	1,079 ± 195	1,079 ± 180	1,080 ± 187	1,074 ± 202	1,051 ± 141	$P = 0.34/0.32$	$P = 0.29/0.13$	$P = 0.99/0.92$
	Accuracy (%)	Simple	98.6 ± 2.5		97.5 ± 3.7	97.7 ± 3.6		97.3 ± 3.7	$P = 0.17$	$P = 0.09$	$P = 0.35$
		Complex	97.1 ± 3.3	98.1 ± 4.3	96.4 ± 6.3	97.8 ± 5.3	97.2 ± 6.7	96.7 ± 5.2	$P = 0.39/0.11$	$P = 0.15/0.40$	$P = 0.09/0.69$
Stroop test	Response time (ms)	Simple	610 ± 82		605 ± 79	608 ± 74		625 ± 100	$P = 0.51$	$P = 0.86$	$P = 0.09$
		Complex	815 ± 173	821 ± 170	810 ± 186	827 ± 168	787 ± 163#	807 ± 162	$P = 0.72/0.75$	$P = 0.60/0.48$	$P < 0.01/0.66$
	Accuracy (%)	Simple	98.1 ± 3.6		97.2 ± 4.9	97.5 ± 3.8		97.1 ± 4.3	$P = 0.60$	$P = 0.31$	$P = 0.77$
		Complex	96.5 ± 4.2	95.8 ± 4.9	95.3 ± 4.9	94.5 ± 5.7	94.2 ± 5.3	95.0 ± 5.7	$P = 0.06/0.06$	$P = 0.43/0.38$	$P = 0.62/0.34$
Corsi blocks	Sequence length		6.3 ± 1.1	6.2 ± 1.0*	6.5 ± 1.0	6.3 ± 1^	5.9 ± 0.9*	5.9 ± 1.1^+	$P = 0.47/0.03$	$P < 0.01/0.39$	$P = 0.09/P < 0.01$
RVIP	Response time (ms)		471 ± 126	503 ± 57	482 ± 113	484 ± 106	466 ± 105	447 ± 123	$P = 0.31/0.41$	$P = 0.40/0.31$	$P = 0.61/0.06$
	Accuracy (%)		49.6 ± 18.4	55.9 ± 17.5*	50.7 ± 19.3	52.5 ± 18.6	52.2 ± 20.1*#	53.1 ± 19.3	$P = 0.07/0.06$	$P < 0.01/0.53$	$P = 0.04/0.64$

*Data is mean ± SD. Pre, Baseline; HT, half-time and FT, full-time. Where tests were completed at half-time and full-time, two P-values are presented; pre to half-time and pre to full-time, respectively. Trial effect (significantly worse on the match = ^), time effect (pre to half-time = * and pre to full-time = &) and interaction effect (half-time con vs. Half-time match = # and full time con vs. full time match = +).*

coefficient (e.g., closer to 1 or –1), the stronger the relationship between the variables. The magnitude of the correlation is deemed small = 0.1, medium = 0.3 and large = 0.5 (Cohen, 1992).

For all analyses, significance was set at $P < 0.05$ and data are presented as mean ± standard deviation.

RESULTS

Cognitive Function

Mean data for all cognitive tests are presented in **Table 1**.

Visual Search

There was no effect of the hockey match on response times or accuracy on the complex level of the visual search test, at half-time or at full-time (all $P > 0.05$). However, response times on the simple level of the visual search test were slower overall during the match trial [main effect of trial, $t_{(1,3,219)} = 2.6$, $P < 0.01$; **Table 1**], globally slowed across time [main effect of time, $t_{(3,3,210)} = 5.6$, $P < 0.01$] and slowed in the control condition from pre-match to full-time whereas they were better maintained in the match trial [trial*time interaction, $t_{(3,3,210)} = -2.9$, $P < 0.01$; ES = –14 ms; **Figure 2C**).

Stroop Test

Response times and accuracy on both the simple and the complex levels of the Stroop test were not affected by the hockey match at full-time (all $P > 0.05$). However, when considering Stroop test performance at half-time, whilst response times were not different overall between the trials (main effect of trial, $P = 0.72$) or across time (main effect of time, $P = 0.60$); there was a significant trial*time interaction, whereby response times improved from pre-match to half-time on the match trial, compared to a slowing in the control trial [trial*time interaction, $t_{(3,4,348)} = -2.8$, $P < 0.01$; ES = –44 ms; **Figure 2A**]. Accuracy on the complex level of the Stroop test was not affected at half-time (all $P > 0.05$).

Rapid Visual Information Processing

There was no effect of the hockey match on response times or accuracy on the RVIP test at full-time (all $P > 0.05$). However, at half-time, whilst response times were not affected (all $P > 0.05$), there was a tendency for accuracy to be greater on the control trial [main effect of trial, $z_{(1,10,654)} = 1.8$, $P = 0.07$] and accuracy was greater at half-time compared to baseline [main effect of time, $z_{(3,10,654)} = 3.4$, $P < 0.01$]. Furthermore, whilst accuracy was similar at half-time compared to baseline on the match trial, accuracy was greater at half-time compared to baseline on the control trial [trial*time interaction, $z_{(3,10,654)} = -2.1$, $P = 0.04$; ES = –6.5%; **Figure 2B**].

Corsi Blocks

The mean length of the 3 longest remembered sequences did not differ between trials from pre match to half-time ($P = 0.47$). From pre-match to half-time sequence length decreased [main effect of time, $F_{(1, 37)} = 7.72$, $P < 0.01$], however no difference was seen between trials in the rate of change [trial*time interaction, $P = 0.09$]. The mean length of the 3 longest remembered sequences was greater in the control trial compared to the match trial [main effect of trial, $F_{(1, 37)} = 4.83$, $P = 0.03$; **Table 1**]. Across time performance did not change (main effect of time, $P = 0.39$). The pattern of change differed from pre-match to full-time, with recall improving on the control trial but decreasing on the match

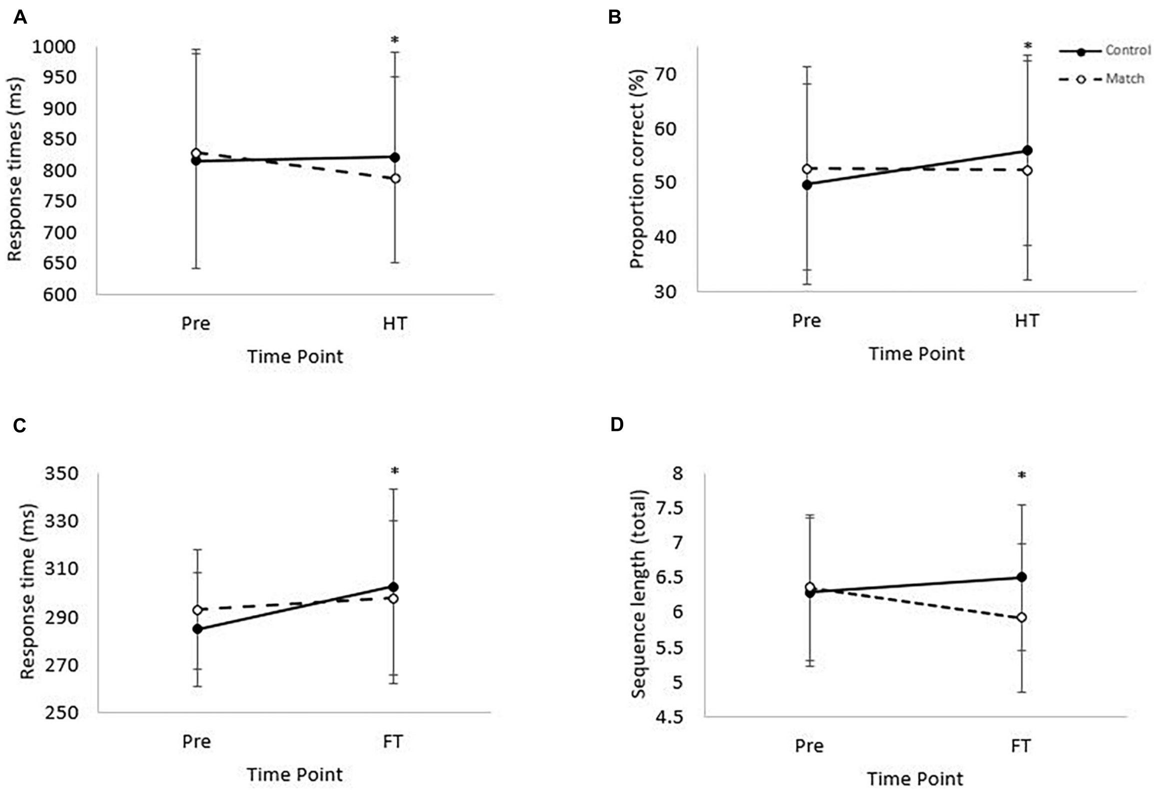

FIGURE 2 | (A) Response times on the complex level of the Stroop test. Pre, prior to the match; HT, half-time. (Trial*time interaction, *$P < 0.01$). Data is mean ± SD. **(B)** Proportion correct on the RVIP test. Trial*time interaction, $P = 0.04$. Pre = baseline and HT = half-time. (Trial*time interaction, $P = 0.04$). Data is mean ± SD. **(C)** Response time on the simple level of the Visual Search test. (Main effect of time, $P < 0.01$; trial*time interaction, $P < 0.01$). Pre, baseline; FT, full-time. Data is mean ± SD. **(D)** Mean sequence length from pre-match to full-time for the Corsi Blocks test. Main effect of trial ($P = 0.03$), and trial*time interaction ($P < 0.01$). Data is mean ± SD.

trial [trial*time interaction, $F_{(1, 37)} = 11.89$, $P < 0.01$; ES = –0.6 blocks, **Figure 2D**].

Hydration Status

Urine osmolality at the beginning of the match trial (567 ± 289 mosmol.kg^{-1}) and the control trial (548 ± 287 mosmol.kg^{-1}) both demonstrated participants were euhydrated upon arrival, with no difference between trials ($P = 0.73$). Body mass change, corrected for fluid intake and urine output, as a percentage of resting body mass, was well maintained and similar between trials (match vs. control: 0.49 ± 1.14 vs. 0.29 ± 0.96%, $P = 0.35$).

Characteristics of the Match

Data for distances run and heart rate across the match can be found in **Table 2**. There was no difference in the distances run at high speed between the first and second half for the men ($P = 0.65$) or the women ($P = 0.81$). High speed meters were positively correlated ($r = 0.42$, $P = 0.04$, *medium effect*) with change in BDNF concentration. Whereas a negative correlation was seen with change in cortisol concentration ($r = –0.40$, $P = 0.048$, *medium effect*). All other correlations (e.g., with cognitive variables) were not significant.

Mood

Raw data for all aspects of mood can be found in **Table 3**. Anger was greater in the match trial [$F_{(1, 35)} = 22.90$, $P < 0.01$] and increased across time [$F_{(1, 35)} = 18.80$, $P < 0.01$]. This led to a significant trial by time interaction [$F_{(1, 35)} = 18.13$, $P < 0.01$], where anger was greater post-match than following the control trial (*post hoc*, $P < 0.01$; d = 1.05, largest effect).

A trial*interaction occurred for confusion [$F_{(1, 35)} = 6.60$, $P = 0.02$], with a higher value for confusion being demonstrated post-match than following the control trial (*post hoc* $P = 0.05$; $d = 0.44$, small effect).

Depression was greater in the match trial [$F_{(1, 35)} = 17.80$, $P < 0.01$] and increased across time [$F_{(1, 35)} = 6.70$, $P = 0.01$]. This resulted in a trial*time interaction [$F_{(1, 35)} = 14.10$, $P = 0.001$], with a significantly higher value for depression being demonstrated post-match than following the control trial (*post hoc* $P < 0.01$; $d = 1.28$, largest effect).

Fatigue increased across time [$F_{(1, 35)} = 19.80$, $P < 0.01$], causing a trial*time interaction [$F_{(1, 35)} = 31.80$, $p < 0.01$], with a higher value for fatigue following the match than following the control trial (*post hoc* $P < 0.01$; $d = 0.81$, largest effect). However fatigue was less at baseline [$t_{(36)} = 2.05$, $P < 0.05$] on the match day trial.

TABLE 2 | Heart Rate and GPS data for male and female athletes.

	1st half	2nd half	Match
Men			
Mean heart rate (beats.min^{-1})	169 ± 7	164 ± 9	–
Max heart rate (beats.min^{-1})	191 ± 6	190 ± 6	–
Total distance (m)		–	6,183 ± 1,589
High speed (m)	–		502 ± 633
Women			
Mean heart rate (beats.min^{-1})	164 ± 19	160 ± 18	–
Max heart rate (beats.min^{-1})	195 ± 10	195 ± 9	–
Total distance (m)	–	–	5,943 ± 1,445
High speed (m)	–	–	493 ± 262

Data is mean ± SD.

TABLE 3 | Mood data for all athletes.

	Control (Pre)	Control (Post)	Match (Pre)	Match (Post)
Anger	4.4 ± 1.0	4.4 ± 1.2$^{\&}$	4.5 ± 1.2^	7.3 ± 3$^{\wedge\&+}$
Confusion	4.6 ± 1.0	4.3 ± 0.6	4.5 ± 0.6	4.9 ± 1.8^{+}
Depression	4.5 ± 1.1	4.1 ± 0.5	4.6 ± 2.5^	6.4 ± 2.5$^{\wedge+}$
Fatigue	8.5 ± 3.3	8.4 ± 3.3$^{\&}$	7.3 ± 2.3	11.1 ± 3.4$^{\&+}$
Tension	5.0 ± 2.4	4.4 ± 1.1$^{\&}$	5.7 ± 1.5^	5.1 ± 1.6$^{\wedge\&}$
Vigor	9.7 ± 3.5	9.5 ± 3.9	11.3 ± 3.0^	10.5 ± 3.9^

Data is mean ± SD. Trial effect (significantly greater than control = ^), time effect (increased from pre to full-time = $^{\&}$) and interaction effect (greater at full time on match vs. con =$^{+}$).

Tension was greater on the match trial (main effect of trial, $F_{(1, 35)} = 8.00$, $P = 0.008$], and decreased across time [main effect of time, $F_{(1, 35)} = 8.00$, $P = 0.008$]. However, no trial*time interaction was present, with a similar pattern of change in both trials.

Vigor was greater in the match trial than the control trial [main effect of trial, $F_{(1, 35)} = 7.80$, $P = 0.008$).

All other findings were non-significant ($P > 0.05$).

Blood Parameters

Data for each blood parameter across the match and control trials are shown in **Table 4**.

Adrenaline

Adrenaline was greater on the match trial [$F_{(1, 30)} = 4.44$, $P = 0.04$], however, no change was seen across time ($P = 0.39$). A trial*time interaction occurred [$F_{(1, 30)} = 5.47$, $P = 0.03$], where adrenaline was greater at the end of the match trial (*post hoc* $P < 0.01$; $d = 0.67$, medium effect).

Noradrenaline

Noradrenaline was greater on the match trial [$F_{(1, 28)} = 13.04$, $P = 0.001$], increased across time [$F_{(1, 28)} = 15.05$, $P = 0.001$]. There was a greater rate of increase from baseline to full-time in the match trial [trial*time interaction, $F_{(1, 28)} = 7.72$, $P = 0.01$, *post hoc* $P < 0.01$; $d = 0.82$, largest effect, **Table 4**].

Cortisol

Cortisol concentration was greater on the match trial [$F_{(1, 25)} = 9.30$, $P < 0.01$]. Cortisol concentration increased on the match trial and decreased on the control trial [trial*time interaction, $F_{(1, 25)} = 22.10$, $P < 0.01$]. Cortisol was greater post-match than following the control trial (*post hoc* $P < 0.01$; $d = 0.85$, largest effect).

Brain Derived Neurotrophic Factor

Overall, serum BDNF was greater on the match trial [$F_{(1, 23)} = 5.70$, $P = 0.03$, **Table 4**]. There was no change across time ($P = 0.15$), resulting in no trial*time interaction ($P = 0.18$).

Oestrogen

There was no difference between the match and control trials for estrogen concentration (control: 767 ± 426 pg.ml^{-1} vs. match: 630 ± 339 pg.ml^{-1}, $P = 0.31$).

Cathepsin B

Cathepsin B did not differ between trials or within trial (all $P > 0.05$).

Correlational Analysis

Correlational analysis revealed a negative correlation between the increase in cortisol and the change in Corsi Blocks performance ($r = -0.314$, $P = 0.01$, *medium*). A negative correlation occurred between the change in noradrenaline and the change in simple level Visual Search response time ($r = -0.284$, $P = 0.01$, *small*). A positive correlation was found between change in cathepsin B and the change in accuracy on the complex level of the Visual Search task ($r = 0.22$, $P = 0.04$, *small*). There were no other statistically significant correlations between the changes in blood parameters and changes in cognitive task performance (all $P > 0.05$).

DISCUSSION

This study was the first to isolate the effects of competitive team sports match on cognitive function. In agreement with the hypothesis, response times were improved on the match trial at half-time for the Stroop test (assessing executive function), compared to the control. However, from pre-match to half-time and full-time, working memory got worse, in comparison to the control. This study provides important implications for how cognition may be influenced across a field hockey match, suggesting a domain specific effect has occurred, and accuracy is not influenced in this process.

The findings of the present study suggest that a competitive field hockey match provides a protective influence on the simple perception test. Therefore, the increment in arousal seen with competitive sport may protect against a drop off in response time, which could be a result of a minimally arousing task being combined with rest on the control trial (Hancock, 1989). For the simple level of the executive function tasks, no changes were seen in response times or accuracy. Whereas on the complex level, response times improved at

TABLE 4 | Blood parameter (mean ± SD) across the control and match day trials.

Blood parameter	Control		Match		Trial effect	Time effect	Interaction effect
	Pre	FT	Pre	FT			
Adrenaline (pg/ml)	96 ± 68	84 ± 48	96 ± 62^	125 ± 71^+	$P = 0.04$	$P = 0.39$	$P = 0.03$
BDNF (serum) (pg/ml)	23,151 ± 9,203	24,423 ± 11,183	26,617 ± 5,472^	29,608 ± 5,933^	$P = 0.03$	$P = 0.15$	$P = 0.18$
Cathepsin B (ng/ml)	67 ± 27	64 ± 24	64 ± 26	66 ± 28	$P = 0.87$	$P = 0.80$	$P = 0.08$
Cortisol (ng/ml)	46 ± 19	33 ± 15&	45 ± 17^	47 ± 18^&+	$P < 0.01$	$P = 0.03$	$P < 0.01$
Noradrenaline (pg/ml)	314 ± 83	348 ± 84&	329 ± 82^	451 ± 156^&+	$P < 0.01$	$P < 0.01$	$P = 0.01$

Pre, Baseline and FT, full-time. Trial effect (significantly greater than control = ^), time effect (increased from pre to full-time = &) and interaction effect (greater at full time on match vs. con =+).

half-time on the match trial when compared to the control trial. Executive function tasks are known to be influenced by the effects of exercise, an effect likely mediated by changes in arousal (Ferris et al., 2007). From a practical standpoint, these changes suggest a player faced with opposing decisions (e.g., dribble or pass) in a game would be able to select the response more quickly. As a result of the selective permeability of the blood-brain barriers, the action of peripheral catecholamines in the central nervous system was warranted to provide a mechanistic explanation for changes seen. Noradrenaline increased across time in the match, which indicates greater activation of central nervous system (McMorris and Graydon, 1996), and likely narrowing of attentional focus (Lemmink and Visscher, 2005). Despite appearing to be domain specific, this alteration in neural function has important implications and is likely to benefit skill performance due to the constantly changing environment. In agreement with the current study, Lemmink and Visscher (2005) also showed improvements in choice reaction time following exercise, implying a narrowing of attentional focus. Despite using a cycling protocol, Lemmink and Visscher (2005) provide a physiological strain which may mimic the transient effects of a section of a match (e.g., time before a rolling substitute). The present study adds to this current literature, providing the most ecologically valid evidence regarding the effects of physiological and psychological strain associated with a team sports match on cognitive performance.

Previously, strong relationships have been demonstrated between both adrenaline and noradrenaline with choice reaction time, which highlights an inverted-U (Chmura et al., 1994). Although only small to medium effect, the correlations seen in the current study confirm that arousal facilitates improvements in perception as the change in response time was negatively correlated with noradrenaline, suggesting that noradrenaline increases alongside improvements in response time.

A decline in working memory was seen at full-time when compared to pre match. Arnsten (2009) suggested increases in noradrenaline awaken neural networks within the prefrontal cortex, influencing working memory in an inverted-U like manner. The inverted-U relationship suggests that the higher intensity, intermittent nature of the competitive sports match in the present study negated the positive effect seen following moderate exercise stress (Martins et al., 2013). A number of studies have highlighted an association between high cortisol levels and poor memory performance (Bohnen et al., 1990; Newcomer et al., 1994), where more recently Quaedflieg and Schwabe (2018) have suggested cortisol can have a positive response depending on the timing of testing in relation to the peak in cortisol. The present study found a medium negative correlation was found between changes in cortisol and working memory, reinforcing the fact that when cortisol increases, working memory decreases (Arnsten, 2009). It is believed that in states of anxiety, when cortisol concentration is increased, the brain preferentially uptakes neurotransmitters associated with emotion over those related to cognitive neurons in the hippocampus and prefrontal cortex (McMorris et al., 2006; Oei et al., 2006; Arnsten, 2009), explaining the cognitive detriment.

Serum BDNF and serum cortisol were overall greater in the match trial, compared to the control trial, which agrees with previous literature where both are greater in response to moderate intensity exercise (Vega et al., 2006). Studies have shown increases in BDNF following high impact anaerobic work to positively influence learning (Winter et al., 2007) and working memory (Griffin et al., 2011). The current findings demonstrate that throughout the match day BDNF is greater than throughout the control trial, which may result in greater BDNF, being secreted from the brain (the hippocampus) and thus enhance neuron health and cognitive performance. However, there is no significant increase across the match in comparison to the control, therefore the mechanisms associated with the change are unclear. Cortisol secretion is known to influence hippocampal neurotrophin expression and synthesis in the brain (de Assis and Gasanov, 2019) if the glucocorticoid receptors are over activated by high loads of cortisol in the blood. This suggests that the lack of change in BDNF across the match may be due to the increasing cortisol concentration throughout the match influencing it's expression.

Mood is known to contribute to changes in cognition (Schmitt et al., 2005). Similar to Moore et al. (2012), the exercise stress in the present study resulted in increases in fatigue, anger, confusion and depression. It is understood that mood has a zone of optimal functioning (Prapavessis, 2000), hence the influence on cognition seen in the current study may indicate that effects of exercise on mood remain within this zone. Further, it has been shown, that changes in mood can enable narrowing of attentional focus, which may have also aided participants to focus on task relevant cues, responding more quickly as a result (Hüttermann and Memmert, 2015). However, the decrement in working memory (corsi blocks performance) at full time coincides with increases in anger, confusion, depression and fatigue, suggesting the domain of working memory is more susceptible to the effects of mood, likely demonstrating a more narrow zone for optimal function.

This study provides a novel approach to assessing the impact of competitive sport on cognition, however, due to the field-based nature and ecological validity, some limitations exist. Due to the time constraints at half-time, a shortened battery of the cognitive tests was conducted. It was decided to complete the more extensive battery at either side of the match despite this, due to the known differences between simple and complex tests (Gaoua et al., 2011; Moore et al., 2012) in response to stress. This process allowed us to get a more thorough understanding of the cognitive responses to competitive sport, whilst still gaining an understanding of how cognition progressed at half time. In a laboratory-based study, the variation in activity patterns between the participants could be deemed a limitation, however, due to the aim of this study being to assess the impact of competitive sport on cognition, this provides the most ecologically valid stimulus to enable us to achieve this. The study used a large sample size spread across positions in order to provide the most accurate insight possible into the physiological demands and resulting influence on cognition.

PRACTICAL APPLICATIONS

Establishing the effects of a competitive team sports match allows further investigation into both, strategies (e.g., nutritional such as caffeine supplementation) which can optimize performance, and stressors which may limit this aspect of performance (e.g., environmental). Incorporating a half-time testing session provides detail to the time course of changes in the varying domains of cognition and highlights the potential for using this break in play as an opportunity to utilize strategies for performance optimization. Although no difference was seen in match variables (high speed meters and total distance run) from the first half to the second half, future research will aim to assess additional measures (e.g., change of direction) which may place greater cognitive, neuromuscular and physiological stress upon players than running meters, and help to explain cognitive changes seen across a match.

CONCLUSION

In conclusion, the present study was the first to isolate the effects of a field hockey match on cognitive function, demonstrating domain and task level (e.g., simple or complex) specific changes in cognition in response to competitive sport. These findings add to the current understanding regarding the potential explanatory variables involved in changes in team sports performance, and provides important implications as to how skill performance may be influenced in a competitive match. Future research must endeavor to elaborate on these findings by investigating the influence of a competitive sport specific protocol, as used in the current study, on sport specific cognitively challenging skills.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author/s.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Nottingham Trent University Invasive Ethics Committee. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

The data was collected in the field at Loughborough University, and then analyzed at Nottingham Trent University. RM, CS, and SC contributed to study design and data collection. CT and JF contributed to study design. RM, CS, SC, CT, and JF contributed to revising the manuscript. All authors approved the final manuscript and listed qualify for authorship and agreed with the order of authorship.

ACKNOWLEDGMENTS

We would like to thank all of the participants for their time and efforts.

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Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

frontiers in Human Neuroscience

ORIGINAL RESEARCH
published: 17 March 2022
doi: 10.3389/fnhum.2022.821261

The Differential Effects of Tai Chi vs. Brisk Walking on Cognitive Function Among Individuals Aged 60 and Greater

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Purpose: The aim of this study was to investigate the differential effects of Tai Chi vs. brisk walking on cognitive function among individuals aged 60 and greater.

Patients and Methods: For participant recruitment, a health talk was arranged at two communities in which two different exercise modalities (Tai Chi and brisk walking) were assigned to participants of each community free of charge. The intervention programs lasted 10 weeks, with three 60-min training sessions per week. General cognitive ability and specific cognitive outcomes were measured using the Chinese version of the Montreal Cognitive Assessment (MoCA).

Results: A significant interaction on total scores of the MoCA was observed ($F = 11.15$, $p < 0.05$). *Post hoc* analysis indicated significant improvements on general cognitive performance as measured in performance on the MoCA for both exercise groups at the end of 10 weeks. A significant interaction was only observed on the delayed recall sub-domain ($F = 12.93$, $p < 0.001$). Results from *post hoc* analysis indicate that the Tai Chi group had a significantly better memory performance relative to brisk walking group ($p < 0.05$). Specifically, significant improvement was observed in Tai Chi group ($p < 0.05$), but not in the brisk walking group. Both exercise groups demonstrated significant improvements from baseline to Week 10, which emerged in visualspatial ability ($p < 0.05$) and attention performance ($p < 0.001$). Lastly, animal naming and orientation significantly benefited from brisk walking ($p < 0.05$) and Tai Chi training ($p < 0.05$), respectively.

Conclusion: Tai Chi and brisk walking as the most commonly used, culture-specific mind-body exercise method have been proven to be effective in improving general cognitive performance and specific cognitive domains. Furthermore, differential effects of two different exercise modalities on cognitive domains were observed, which has provided insightful information for customized exercise programs. Finally, aging individuals who are experiencing cognitive decline should either take Tai Chi classes regularly or engage in brisk walking, which could contribute to brain health.

Keywords: Tai Chi, exercise, cognition, memory, old people

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Edited by:
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Specialty section:
This article was submitted to Cognitive Neuroscience, a section of the journal Frontiers in Human Neuroscience

Received: *24 November 2021*
Accepted: *10 February 2022*
Published: *17 March 2022*

Citation:
Yu Y, Zuo E and Doig S (2022) The Differential Effects of Tai Chi vs. Brisk Walking on Cognitive Function Among Individuals Aged 60 and Greater. Front. Hum. Neurosci. 16:821261. doi: 10.3389/fnhum.2022.821261

INTRODUCTION

The number of individuals aged 60 years old and greater is significantly increasing, with data from the world Health Organization indicating 1 billion in 2019. The global proportion of this age group will contiguously elevate and reach 1.4 billion by 2030 (Miniscalco et al., 2006). To be consistent with the global trend in population aging, China–a developing country–is also undergoing a significant increase (Han et al., 2020). Data has indicated that individuals aged 60 years and over had reached roughly 250 million in 2018, accounting for about 18% of the total population (Chunli, 2019). This aging population is facing health challenges, particularly a widely recognized decline on cognitive function (refer to multiple mental skills including attentional ability, memory, language, executive function/visuospatial ability) (Zou et al., 2019a). Such age-related cognitive decline could generate substantial economic burdens and affect the personal life of an individual. Thus, looking for approaches to mitigate the progress of cognitive decline with normal aging is urgently needed.

Until now, pharmacological methods have been found to be ineffective at reversing age-related cognitive decline, with many reporting side effects following use of these drugs (Andrade and Radhakrishnan, 2009). Against this background, some researchers have started to shift their attention to modifiable lifestyle factors including smoking, alcohol use, and physical activity. Of them, physical activity has been observed as an effective approach to improve cognitive function of aging populations with healthy individuals or those with cognitive impairment (Demurtas et al., 2020). For example, multiple meta-analytical reviews conducted by several research groups indicated that exercise improved cognitive function among middle-aged and older individuals (Kelly et al., 2014; Northey et al., 2018; Sanders et al., 2019; Wu et al., 2019). Physical activity refers to musculoskeletal behaviors with energy expenditure. It contains a wide range of modalities such as aerobic exercise, resistance training, endurance training, high-interval intensity training. Under the umbrella of exercise, the superior effects on cognitive function were observed following mind-body exercises (Tai Chi, and Yoga) (Herold et al., 2018; Wu et al., 2019; Yu et al., 2021). Furthermore, Tai Chi as a unique exercise modality has recently gained increased global popularity, especially among older individuals, which may be attributed to the slow and gentle movements, deep breathing techniques, and sensorimotor training.

With the increasing number of experimental studies investigating the cognitive benefits of mind-body exercises among aging populations, several reviews were conducted, indicating that mind-body exercises have the potential to improve cognitive functioning in older individuals (Wu et al., 2013; Wang et al., 2018; Lim et al., 2019). Of note, the majority of these previous studies focused on single mind-body exercise vs. non-active control or the comparative effects of two different types of mind-body exercises (Zou et al., 2019b). Very few studies have investigated the differential effects of exercise type on cognitive function in elderly populations (Demurtas et al., 2020). A cross-sectional study was recently published (Yue et al., 2020), indicating that as compared to older adults who engaged in brisk walking for at least 5 years (60 min × 5 times per week) Tai Chi practitioners demonstrated significantly better behavioral measure/cognitive function (delayed recall-memory function) and greater hippocampus. Researchers concluded that such superior effects may be attributed to complexity of Tai Chi movements (motor-coordinative training and movement sequence) and mindfulness-based training. Given that results from a cross-sectional study cannot establish a cause-and-effect relationship, more experimental studies are needed to substantiate this promising finding. Thus, the aim of this study was to investigate the effects of Tai Chi vs. brisk walking on cognitive function among older individuals aged 60 and over. Results from this study would provide insightful information for health professionals to customize exercise training regiments among healthy older adults who suffer normal cognitive decline.

MATERIALS AND METHODS

Study Participants and Group Assignment

In the present study, an experimental design was used to investigate the effects of Tai Chi vs. Brisk Walking on cognitive function among individuals aged 60 and greater. For participant recruitment, a health talk was arranged at two different communities in which only information about physical and physiological benefits of exercise was presented but not brain health (to minimize the social desirability). To be included in this study, individuals must meet the inclusion criteria: (a) healthy participants at the age of 60 or greater; (b) able to walk independently and perform daily living activities–which would allow participants to successfully learn Tai Chi forms; (c) baseline MoCA [the Montreal Cognitive Assessment Scale] scores should reach at least 26, which reflects normal cognitive level. Likewise, individuals who were interested in this study but belong to one of the following criteria were excluded: (a) being diagnosed with any major diseases like stroke, heart attack, chronic obstructive pulmonary disease, or diabetes mellitus; (b) hearing and/or vision impairments which would limit their ability to follow instruction during exercise training and assessment; (c) engagement in any behavioral or exercise training program in previous 2 months. Two different types of exercise modalities were arranged at two communities in which one group attended Tai Chi and another engaged in brisk walking. Study protocol (PN-2020-034) was approved by the Xiangnan University ethical committee.

Exercise Training Modalities

Participants who volunteered to participate in Tai Chi training were informed about the intervention duration, frequency of outcome measures, and associated policies. Specifically, Tai Chi intervention duration lasted 10 weeks (60-min training session × 3 times per week) in which 24-style form was taught by two certified instructors (Zou et al., 2019b). Prior to each Tai Chi training session, an 8-min warm up was arranged including whole-body stretching and footwork training (the foundation for Tai Chi form practice). And then participants learned Tai

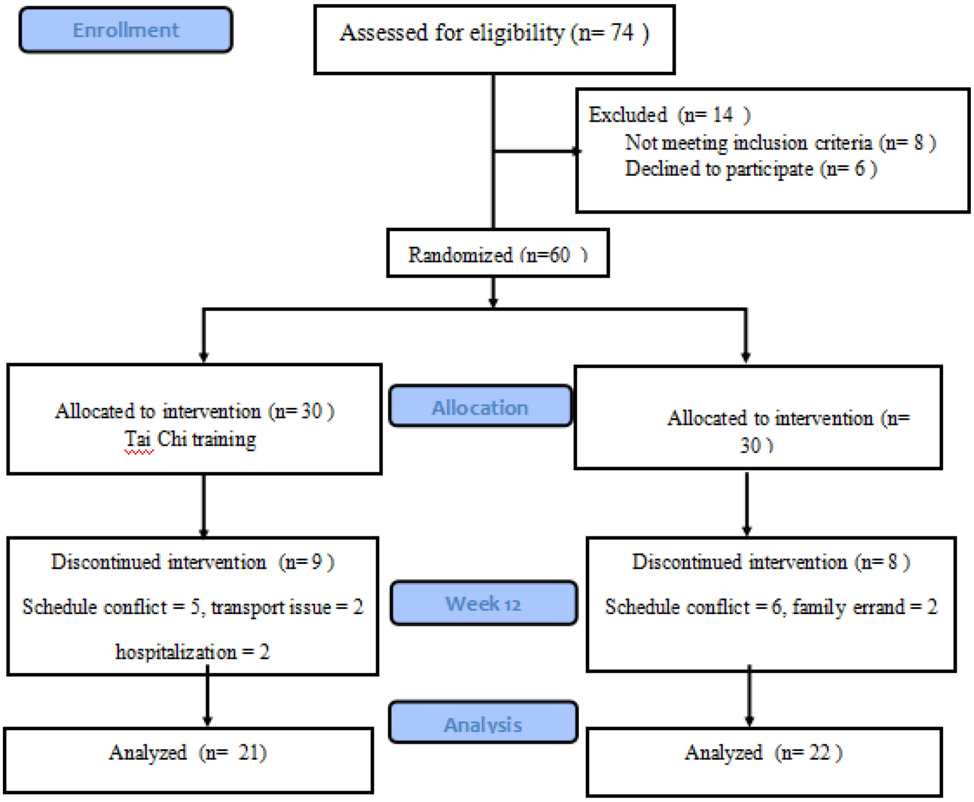

FIGURE 1 | Flowchart of enrollment, baseline, and post-assessment.

Chi moves and memorized its associated movement sequences, followed by another 5-min cool-down section. To maximize the teaching effectiveness and quality, Tai Chi groups were separated into groups of 15 participants. To be consistent in terms of teaching, two instructors were given time to communicate with each other after their own Tai Chi training session. Participants in the brisk walking group underwent the same intervention duration in which they received 60-min walking sessions 3 times per week. All brisk walking sessions were instructed by a sophisticated instructor who engaged in outdoor sports for 20 years. Of note, the heart rate was collected in one-third of each group to monitor the exercise intensity; 65–75% of the maximum heart rate (220–age) was targeted zone.

Outcome Assessment

Demographic data were collected in the present study, including age, gender, educational level, handedness, height, and weight (can be calculated for BMI). Of note, this information was self-reported. Global cognitive function and its associated subdomains were measured using MoCA.

The Chinese version of the Montreal Cognitive Assessment (MoCA) was used to measure global cognitive performance and its individual abilities (Lu et al., 2011), which was administered by trained research assistants. This assessment tool consisted of 30 items within the following domains: Orientation, delayed recall, visuospatial ability/executive functioning, language abilities, abstraction, animal naming, attention, and clock-drawing test. It took approximately 12–15 min to complete the entire assessment. Each participant could obtain a maximum of 30 points. Individual scores across domains ranged between 3 and 6: (a) to assess orientation [6 points], participants were asked to state the date, month, year, day, place, and city; (b) delayed recall [5 points] was assessed; (c) executive function/visuospatial ability [5 points] were measured *via* Trail Making B–participants were asked to draw a line to correctly connect alternating digits and numbers like 1-A and 2-B; (d) language abilities [3 points] required participants to repeat two sentences correctly and then list all of the words that could be recalled starting with the Letter F; (e) to measure abstract reasoning [2 points], participants were asked to explain how two items were alike [train and bicycle]; (f) the animal naming test [3 points] consisted of three pictures of animals presented to participants who were asked to name each item; (g) the attention task [6 points] was comprised of a series of numbers which participants were asked to recite forward and backward.

Experimental Procedures

A health talk was arranged at two different communities in which the majority of audiences were older adults aged sixty and greater. Immediately after this event, participants were invited to attend one of the exercise programs. Only those who met the eligibility requirements completed the baseline

TABLE 1 | Demographic information.

Demographic	Tai Chi	Brisk walking	Statistic (df)	*p*-value
Gender			$\chi 2(1) = 0.196$	0.658
Male	10 (47.6%)	9 (40.9%)		
Female	11 (52.4%)	13 (59.1%)		
Educational Level			$\chi 2(1) = 0.305$	0.859
College or greater	5 (23.8%)	6 (27.3%)		
Associate degree	13 (61.9%)	14 (63.6%)		
High school or below	3 (14.3%)	2 (9.1%)		
Age (years)	64.90 ± 3.37	66.86 ± 5.74		0.183
BMI (kg/m2)	24.03 ± 1.48	23.23 ± 2.74		0.242
MoCA	26.38 ± 1.35	26.59 ± 1.40		0.513

MoCA, Montreal cognitive assessment.

assessment. Eligible participants were informed that they could withdraw from the 10-week intervention exercise program at any time. Post-assessment was also performed after the 10-week intervention period within one week. Trained graduate students were responsible for cognitive assessments. Nine participants (5 males and 4 females) did not complete the 10-week Tai Chi intervention due to the following reasons: (a) schedule conflicts = 5 participants; (b) hospitalization = 2 participants; (c) transport issue = 2 participants. Similarly, participants in the Brisk Walking group dropped out because of: (a) schedule conflicts = 6 participants; (b) family errand = 2 participants. Procedures are detailed in **Figure 1**.

Statistical Analysis

Demographic data, MoCA and its associated sub-domain scores were collected for baseline analyses. The number and percentage were used to present results of categorical variables while mean and standard deviation (SD) were reported for continuous variables. A chi-square test and independent *t*-test were used for categorical and continuous variables, respectively. A two-way ANOVA with repeated measure was conducted to investigate the effects of Tai Chi vs. brisk walking on cognitive function. *Post hoc* analysis was carried out using a Bonferroni test when significant main and group × time interaction effects were found. A *p* value of less than 0.05 was used to determine significance level.

Patient and Public Involvement

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

RESULTS

The number of male and female participants in both exercise groups were relatively equal ($p = 0.658$). Specifically, there were 10 male participants in Tai Chi group, accounting for 47.6% of the total number, while 9 male participants (40.9%) engaged in brisk walking training. With respect to educational level, a relatively equal number of participants across three different educational levels were observed ($p = 0.859$). Participants in the Tai Chi group had a mean age of 64.90 ± 3.37 years old, while the brisk walking group was 66.86 ± 5.74; no significant group difference was observed on age. BMI of Tai Chi and brisk walking were 24.03and 23.23 kg/m2, respectively. No significant difference between Tai Chi (26.38 ± 1.35) and brisk walking (26.59 ± 1.40) groups was observed in baseline MoCA scores ($p = 0.513$). Participant descriptive statistics are detailed in **Table 1**.

A significant interaction on total scores of the MoCA was observed ($F = 11.15$, $p < 0.05$). Results from *post hoc* analysis indicate significant improvements on general cognitive performance as measured by the MoCA in both exercise groups for Week 10 of the intervention.

With respect to sub-domains, only a significant interaction on delayed recall was observed ($F = 12.93$, $p < 0.001$). Results from *post hoc* analysis indicate that Tai Chi group had significantly better memory performance relative to Brisk Walking group ($p < 0.05$). Specifically, significant improvement was only observed in Tai Chi group ($p < 0.05$), but not in the Brisk Walking group. Both exercise groups demonstrated significant improvements from Week 10 to baseline, which emerged in only visualspatial ability ($p < 0.05$) and attention performance ($p < 0.001$). Lastly, animal naming and orientation significantly benefited from Brisk Walking ($p < 0.05$) and Tai Chi training ($p < 0.05$), respectively. Subdomain scores are detailed in **Table 2**.

DISCUSSION

In the present study, researchers have investigated the effects of two different exercise modalities on cognitive function among individuals aged 60 and greater. Specifically, this quasi-experimental study not only focused on general cognitive performance following the 10-week Tai Chi and Brisk Walking training, but researchers were also interested in its associated cognitive domains. Results of this study indicated that individuals who were at the age of 60 can receive cognitive benefits following both exercise modalities, with differential effects on specific cognitive domains. Potential mechanism of exercise-induced cognitive benefits will be discussed below.

As mentioned previously, age-related cognitive decline has been widely recognized, which typically deteriorates (converting to dementia) without any preventive strategies. To this end, researchers and health professionals have been searching for effective approaches to decelerate the progress of cognitive decline and improve brain health to lead to a better quality of life. When the etiology of cognitive decline remains largely unclear, associations with modifiable lifestyle behaviors and cognitive function for aging populations have attracted greater attention from the research community. Of these modifiable lifestyle factors, physical activity or exercise is of particular research interest. Specifically, researchers have investigated the cognitive benefits of acute and chronic exercise among aging populations. Accumulating evidence indicate the beneficial effects of aerobic exercise and resistance training for cognitive improvement and brain health. Recently, researchers have started to investigate the effects of mind-body exercise (Tai Chi, Yoga, and Baduanjin Qigong) on cognitive function in aging populations. Such exercise modality has gained increasing popularity globally,

TABLE 2 | Montreal cognitive assessment and its associated sub-domain scores.

Outcomes	Tai Chi		Brisk walking		*F*-value	
	Baseline	Week 1.0	Baseline	Week 10	Group	Group × Time
MoCA	26.38 ± 1.35	29.33 ± 0.73**	26.59 ± 1.40	28.32 ± 1.21**	3.48	11.15*
Visuospatial Ability	4.62 ± 0.67	4.90 ± 0.30*	4.55 ± 0.74	4.82 ± 0.39*	0.295	0.006
Animal Naming	2.86 ± 0.35	3.00 ± 0	2.73 ± 0.46	3.00 ± 0*	1.071	1.07
Attention	4.71 ± 0.78	5.86 ± 0.36**	4.64 ± 0.90	5.5 ± 0.67**	1.396	1.48
Language Ability	2.76 ± 0.54	2.90 ± 0.3	2.86 ± 0.35	2.91 ± 0.29	0.395	0.36
Abstraction	1.95 ± 0.22	2.0 ± 0	1.82 ± 0.39	1.82 ± 0.39	3.653	0.34
Delayed Recall	4.10 ± 0.83	4.81 ± 0.40*	4.77 ± 0.43	4.82 ± 0.39	6.26*	12.93**
Orientation	5.38 ± 0.50	5.86 ± 0.36*	5.23 ± 0.69	5.46 ± 0.67	3.53	1.81

*MoCA, Montreal cognitive assessment; *, $p < 0.05$; **, $p < 0.001$.*

especially among aging populations–it is mainly attributed to slow pace movement features which older practitioners can follow. In addition, deep breathing practice could help to alleviate negative emotion and loneliness experienced by older individuals.

After the 10-week intervention period, Tai Chi and brisk walking training programs effectively improved visualspatial ability and attention ability. Such results of the present study are in line with previous studies (Muiñs and Ballesteros, 2018; Zou et al., 2019a; Nemoto et al., 2020). For example, Tai Chi has a greater emphasis on eye-hand-feet coordination in which participants were required to place their feet correctly and dynamically carry out weight shifting in order to maintain balance. Visualspatial ability and attention was consistently trained throughout the 10-week intervention period. Interestingly, Brisk Walking and Tai Chi training improved animal naming and orientation, respectively. Brisk Walking training was performed as a group in which participants had the opportunity to communicate, which possibly had positive effects on this outcome. As mentioned previously, Tai Chi form involved multi-directional movement, which resulted in better performance in the orientation task. With respect to delayed recall, Tai Chi group demonstrated better memory performance relative to brisk Walking group. Furthermore, the significant improvement was only observed in Tai Chi group, but not in the Brisk Walking group. Findings suggest that Tai Chi may have the superior effects on memory function, which is supported by a previous study (Zou et al., 2019a). Such results may be attributed to unique features which require participants to memorize movement sequences during Tai Chi training in comparison with brisk walking that only involved simple movement patterns. Unsurprisingly, improvements in multiple subdomains were observed, which in turn contributed to significantly greater general cognitive performance (as measured by the MoCA) at Week 10 relative to baseline.

Tai Chi training-induced cognitive function may be also attributed to molecular and cellular changes (first level) as well as functional and structural brain changes (second level) (Brown et al., 2013; Gomez-Pinilla and Hillman, 2013; Marmeleira, 2013; Norman et al., 2018). With respect to the first level, brain-derived neurotrophic factor (BDNF) and other neurotrophic factors have been increasingly recognized to associate with cognitive function. A significant number of animal and human studies indicated that regular exercisers with greater aerobic fitness was associated with basal levels of BDNF, which contributed to larger hippocampal volume and better memory function (Currie et al., 2009; Erickson et al., 2010, 2011). Specifically, a well-designed study investigated the effects of Tai Chi on cognition and associated plasma biomarkers among older adults with amnestic mild cognitive impairment (Sungkarat et al., 2018). After a 6-month intervention period, in comparison with a control group, Tai Chi group demonstrated significantly better memory performance and executive function, which was mediated by an upregulation of BDNF. Thus, 12-week Tai Chi training can improve aerobic fitness and elevate BDNF levels, which in turn facilitates memory performance enhancement. When taking a look at the second level, a leading study conducted by Erickson indicated that aerobic exercise can increase the size of the hippocampus and enhance memory performance following a 12-month intervention period (Erickson et al., 2011). In this study, a total of 120 older individuals were randomly assigned into either aerobic exercise (3 × 60 min per week) or stretching control; memory function and brain structure were measured across three time points. Interestingly, older participants in the aerobic exercise group demonstrated significantly increased size of the anterior hippocampus (2%), which effectively reverse this brain structure loss due to normal aging. Furthermore, this study reported greater size of hippocampus was linked to higher serum levels of BDNF. Such brain structure change and molecular change ultimately led to significant improvement in spatial memory performance. Collectively, Tai Chi training-induced cognitive benefit may be due to the BDNF and the increased size of hippocampus.

Strengths and Limitations

Tai Chi as a mind-body exercise has been identified to improve cognitive function of aging population. Culture-specific Tai Chi and Brisk Walking are easy-to-learn in Chinese society, especially in aging populations who commonly used such exercises for health benefits. Investigation on the cognitive benefits of Tai Chi vs. Brisk Walking have rarely been done simultaneously. Thus, results of the present study have added value to the existing literature. Several limitations in this study should be admitted. Firstly, this is a non-randomized controlled trial in which participants in both groups may have high expectations. To further verify the positive effects of Tai Chi on cognitive function of the elderly, future studies on this similar topic should include at least a wait-list control group. Secondly, individuals aged 60 and greater were commonly reported with depression and loneliness that were not measured in this study. It remains unclear if exercise-induced effects could alleviate these negative emotions, leading to better cognitive performance. Thirdly, this study only included assessments of baseline and post-intervention. Further investigation is required to assess if such positive effects persisted past the end of the study. Fourth, blinding of assessors may also confound the results of the present study. Fifth, economical level of participants were not collected in this study, which requires attention in the future studies. Lastly, a non-active control should be added in future studies so that results on the beneficial effects of two exercise modalities are more persuasive.

CONCLUSION

Tai Chi and brisk walking as the culture-specific mind-body exercise and the most commonly used method have been proven to be effective in improving general cognitive performance and specific cognitive domains. Furthermore, the differential effects of two different exercise modalities on cognitive domains are observed, which has provided insightful information for customized exercise programs. Finally, aging individuals who are experiencing cognitive decline should either take Tai Chi classes regularly or engage in brisk walking, which could contribute to brain health.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Xiangnan University Ethics Committee. Informed consent was obtained from all subjects involved in the study prior to the starting of this study.

AUTHOR CONTRIBUTIONS

YY and EZ: conceptualization, validation, investigation, and data curation. YY and SD: methodology and formal analysis. YY: software and resources. YY, EZ, and SD: writing—original draft preparation and writing—review and editing. EZ: visualization, supervision, project administration, and funding acquisition. All authors have read and agreed to the published version of the manuscript.

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frontiers | Frontiers in Human Neuroscience

ORIGINAL RESEARCH
published: 24 June 2022
doi: 10.3389/fnhum.2022.894911

Behavioral and Brain Reactivity Associated With Drug-Related and Non-Drug-Related Emotional Stimuli in Methamphetamine Addicts

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Background: Methamphetamine addicts can experience severe emotional processing disorders, with abnormal responses to emotional and drug-related stimuli. These aberrant behaviors are one of the key factors leading to relapse. Nevertheless, the characteristics of addicts' responses to drug-related stimuli and their responses to emotional stimuli remain controversial.

Methods: 52 methamphetamine addicts from China passively viewed three different categories of images: Drug-related; positive emotional; and negative emotional. In the first task, participants completed a 9-point Self-Assessment Manikin (SAM) scale, rating the valence of each image. In the second, they performed a cued-action task while electroencephalography (EEG) data were recorded.

Result: Drug-related images were rated negatively, with an average rating of 3.57. However, reaction times to drug-related stimuli were significantly faster than for negative stimuli ($p = 0.030$), and were indistinguishable from positive stimuli ($p > 0.99$). Similarly, EPN amplitudes evoked by drug-related images were significantly larger than those evoked by negative stimuli ($p < 0.001$), but no different than positive stimuli ($p > 0.99$). LPP amplitudes evoked by drug-related stimuli were significantly smaller than those evoked by negative ($p < 0.001$) and positive stimuli ($p = 0.004$).

Conclusion: Despite negative self-assessments of drug-related imagery, MA-addicts reaction times were no slower than positive reactions. Similarly, drug-related and positive imagery EPN amplitudes were indistinguishable. Together, these results suggest increased attentional resources were allocated to the processing of drug-related stimuli and the pathways responsible partially overlap with the those recruited in processing positive emotional imagery in addicts. Moreover, in the late stage of visual processing, MA-addicts showed reduced brain activity in response to drug-related stimuli, suggesting reverse inhibition in response preparation and emotional appraisal. These findings may provide a reference for clinicians treating drug-taking behavior and for the development of new models of rehabilitation therapy.

Keywords: methamphetamine addiction, emotion, P1, EPN, LPP

OPEN ACCESS

Edited by:
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Specialty section:
This article was submitted to Cognitive Neuroscience, a section of the journal Frontiers in Human Neuroscience

Received: *07 April 2022*
Accepted: *08 June 2022*
Published: *24 June 2022*

Citation:
Li X, Zhou Y, Zhang G, Lu Y, Zhou C and Wang H (2022) Behavioral and Brain Reactivity Associated With Drug-Related and Non-Drug-Related Emotional Stimuli in Methamphetamine Addicts. Front. Hum. Neurosci. 16:894911. doi: 10.3389/fnhum.2022.894911

INTRODUCTION

Methamphetamine (MA) is a synthetic drug whose use has become increasingly prevalent in many countries, causing great harm to society, families, and individuals. Evidence shows that persons with MA dependency have higher rates of suicide and comorbidity, and are more likely to commit crimes (Marshall and Werb, 2010; Argento et al., 2017; Liu et al., 2017). Addicts often exhibit both impulsive and compulsive behaviors. In particular, they engage in compulsive drug taking despite the desire to stop taking the drug (Degoulet et al., 2021). Even after long periods of withdrawal treatment, once re-exposed to the drug environment, addicts are prone to relapse (Bechard and Knackstedt, 2019). Tackling these aberrant behaviors is key to the successful treatment of drug addiction.

Addicts also show severe emotional processing disorders, often experiencing abnormal emotional responses (Rabin et al., 2021; Warlow and Berridge, 2021). For example, long-term use of MA may lead to dysfunction of neural circuitry in the prefrontal and limbic systems (Feng et al., 2018). As a consequence, addicts show reduced arousal in response to non–drug-related positive emotional stimuli (May et al., 2020) and, concurrently, must increase the dose of the drug to maintain the same degree of pleasure (Volkow et al., 2011, 2016). Addicts may also have greater sensitivity to non–drug-related negative emotional stimuli, thus displaying higher incidences of depression and moodiness (Moustafa et al., 2020), which may lead to relapse. Therefore, if we wish to prevent relapse, understanding behavioral and neurological responses to emotional stimuli is paramount.

From an evolutionary perspective, human behavior is motivated by appetitive and defensive systems (Bradley et al., 2001; Lang and Bradley, 2010). Put simply, people approach positive stimuli and avoid negative stimuli. Compulsive drug taking can be considered an approach behavior, thus one might expect the addict's response to drug-related stimuli to be consistent with their response to positive stimuli. However, long-term use of MA can cause addicts to experience strong negative emotions such as anxiety, depression, and anger (Alamdarloo et al., 2019; May et al., 2020). In addition, addicts learn about the dangers of drugs through drug-related laws and regulations, and social evaluations (Liu et al., 2018). Over time, these factors may cause addicts to react adversely to drug-related stimuli. Indeed, drug addicts tend to rate drug-related stimuli negatively (Wang et al., 2015). Given this discrepancy, further research is needed to elucidate the mechanisms underlying addicts' responses to drug-related stimuli.

In recent years there has been a proliferation of research examining the neural processing of drug-related stimuli. For example, studies using functional magnetic resonance imaging (Costumero et al., 2018) and electroencephalography (EEG) (Motlagh et al., 2017; Bu et al., 2019) have demonstrated that compared with healthy controls, drug-dependent individuals show enhanced brain activity while looking at images associated with drugs. Moreover, adjacent research has found that brain activity elicited by drug-related stimuli is enhanced compared with that induced by general emotional stimuli (Marianne and Franken, 2011; Yang et al., 2015). This has not been without controversy, however, and other research has observed significant differences in brain activity only between drug-related stimuli and neutral stimuli, not between drug-related stimuli and emotional stimuli (Francesco et al., 2015).

In the present study, we investigated behavioral and neural responses to drug-related stimuli using a Self-Assessment Manikin (SAM) scale, and a cued-action task in conjunction with EEG. More specifically, we assessed the difference between responses to drug-related stimuli and non–drug-related positive or negative emotional stimuli, in MA-addicts who were currently MA-abstinent. Participants completed a SAM scale and a cued action task (the latter while wearing EEG electrodes) after passively viewing images that were either drug-related or non–drug-related emotional images. Previous studies have shown negative emotion slows reaction times, whereas positive emotion leads to faster reaction times (Beatty et al., 2016; Li et al., 2019). We analyzed EEG event-related potentials (ERPs), including P1, early posterior negativity (EPN), and the late positive potential (LPP). These three components are closely related to emotional stimulus processing, with ERP amplitudes previously associated with emotional stimuli (Aftanas et al., 1998; Flaisch et al., 2010; Lu et al., 2021). We hypothesized that both MA-addicts' behavioral and neural responses to drug-related stimuli would differ from those associated with non–drug-related emotional stimuli.

MATERIALS AND METHODS

Participants

In total, 52 MA-addicts (with 3 months of abstinence) were enrolled through the Drug Rehabilitation Bureau of Zhejiang Province. All participants were native Chinese men aged between 18 and 45 years, met the *Diagnostic and Statistical Manual of Mental Disorders* (Fifth Edition) criteria for a current MA use disorder, had no self-reported history of mental illness or chronic physical illness, were right-handed, and had normal or corrected-to-normal vision. **Table 1** summarizes the demographic characteristics of the participants.

The present study was approved by the ethics committee of Shanghai University of Sport (No. 102772019RT041) and conducted in accordance with this approval. Written, informed consent was obtained from all participants prior to their participation and confidentiality was upheld at all times.

Materials

The present study used 195 images, of which 130 images were selected from the Chinese Affective Picture System (65 images were associated with positive emotions, and 65 with negative emotions) (Lu et al., 2005) and 65 MA-related images were selected from available online sources. All images were aligned in size and luminance. The formal experiment utilized 180 images (60 positive, 60 negative, and 60 MA-related), with the remaining 15 used to familiarize participants with instructions.

The images were assessed for valence and arousal on a 9-point Self-Assessment Manikin (SAM) scale by 30 MA-addicts

TABLE 1 | Demographic and drug-taking characteristics of the study sample.

Variable	Mean (*SD*)
Age (years)	34.7 (6.7)
Educational level (years)	8.7 (1.7)
Methamphetamine dependency (years)	6.1 (3.5)
Frequency of use (day/week)	2.6 (2.2)
Amount of use (gram/dose)	0.4 (0.4)

Drug-taking habits reflect those prior to rehabilitation and abstinence.

who were not participants in the formal experiment to assess the suitability of our SAM measure (**Table 2**).

Two one-way repeated measures ANOVAs were conducted to compare valence and arousal, respectively, between the three levels of emotional stimuli. We found there was an effect of emotion type on valence [$F_{(2,\ 28)} = 62.836$, $p < 0.001$]. More specifically, *Post hoc* pairwise *t*-tests (Bonferroni corrected) revealed positive ($M = 6.66$, $SD = 1.15$) emotional stimuli had greater valence than negative ($M = 2.78$, $SD = 1.10$) stimuli ($p < 0.001$) and MA-related ($M = 3.30$, $SD = 1.63$) stimuli ($p < 0.001$). In addition, there was no significant difference between the valence of the MA-related stimuli and the valence of the negative stimuli ($p = 0.176$). We also found an effect of emotion type on arousal [$F_{(2,\ 28)} = 12.899$, $p < 0.001$]. *Post hoc* pairwise *t*-tests (Bonferroni corrected) revealed negative ($M = 6.37$, $SD = 1.35$) stimuli had higher arousal ratings than positive ($M = 5.30$, $SD = 0.96$) stimuli ($p < 0.05$), which, in turn, had significantly higher arousal ratings than MA-related ($M = 4.30$, $SD = 1.98$) imagery ($p < 0.05$). The difference between positive and MA-related stimuli was not significant ($p = 0.056$).

Design and Procedure

The experiment consisted of two tasks, both of which were a repeated-measures design with stimulus type (positive, negative, and MA-related images) as the factor. Each condition consisted of 60 images.

For task 1, each trial began with a fixation cross presented on the computer screen for between 500 and 700 ms, drawn randomly from a uniform distribution. This screen was followed by a 1,200 ms presentation of one of the three image types. Participants were instructed to look carefully at the image. After the image disappeared, participants were asked to rate the valence of the image on a 9-point SAM scale using the keyboard (1 = very unpleasant; 9 = very pleasant). A blank screen was then presented for 800 ms before concluding the trial (**Figure 1**). The order of stimulus presentation was random.

TABLE 2 | The SAM ratings of emotional pictures.

Emotion type	Valence *M* (SD)	Arousal *M* (SD)
Negative	2.78 (1.10)	6.37 (1.35)
Positive	6.66 (1.15)	5.30 (0.96)
MA-related	3.30 (1.63)	4.30 (1.98)

Task 2 combined electroencephalography (EEG) with a cued-action task. Participants were seated approximately 60 cm from a computer in a dimly lit, quiet room. After participants had been introduced to the experiment, EEG electrodes were attached to them. During the experiment, a fixation cross was presented on the computer screen for between 500 and 700 ms, drawn at random from a uniform distribution. This screen was followed by a 1,200 ms presentation of one of the three image types. After the image disappeared, a black bar appeared on the screen to cue participants that an action was required. Participants were instructed to click on the black bar as soon as possible using their mouse, and then click a button labeled "submit." A blank screen was then presented for 800 ms (**Figure 1**). Once again, the stimulus presentation order was random. The task procedure was compiled and run using E-Prime 2.0 software.

Behavioral Data Acquisition and Analyses

Behavioral data consisted of rating scores from the 9-point SAM scale and reaction times from the cued-action task. Reaction times were computed as the time elapsed between when the black bar appeared on the screen, and when the participant clicked on it. Rating scores and reaction times were analyzed by one-way repeated-measures analyses of variance (ANOVAs) with image type (positive, negative, and MA-related) as main effects. *Post hoc* pairwise *t*-tests (Bonferroni corrected) were then run on any significant main effect. Statistical analyses were performed in SPSS, version 22.0 (IBM Inc.).

Electroencephalography Data Acquisition and Analyses

EEG data from task 2 was collected with 64 Ag-AgCl electrodes arranged according to the international 10–20 system, with a sampling frequency of 1,000 Hz (Brain Products GmbH 64, Germany). The EEG was recorded referentially against the FCz electrode, and AFz served as the ground electrode. The vertical electrooculogram was recorded infraorbitally at the left eye, and the horizontal electrooculogram was recorded lateral to the orbit of the right eye. All electrooculogram and EEG electrode impedances were maintained at less than 5 kΩ.

Time-domain analyses were used to analyze the EEG data. We processed EEG data using a Brain Vision Analyzer2 (Germany). FCz was re-referenced to the average of the TP9 and TP10 electrodes. Ocular artifacts were then removed through ocular correction. Next, we removed line noise with a 50-Hz notch filter. Then, the data were filtered with a 30-Hz low-pass cutoff and a 0.5-Hz high-pass cutoff. The data were then segmented from 200 ms prior to the onset of the image to 1,000 ms after the image onset. All epochs were baseline-corrected with respect to the mean voltage over the −200 to 0 ms period preceding image onset and then averaged by experimental condition. Trials with amplitudes exceeding $\pm$ 80 μV were considered artifacts and thus excluded. P1, EPN, and LPP were selected as target ERP components. We analyzed the averaged P1 amplitude at the occipital-temporal electrodes PO7, PO8, O1, and O2 within the time window of 130–170 ms, the averaged EPN at electrodes

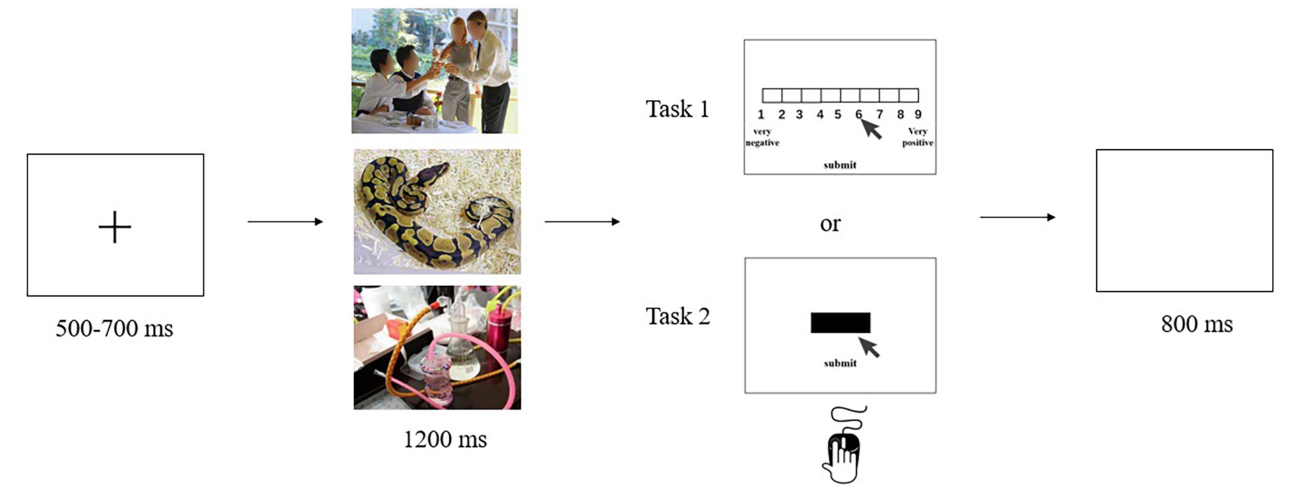

FIGURE 1 | The 9-point SAM rating task (task 1) and the cued-action task (task 2).

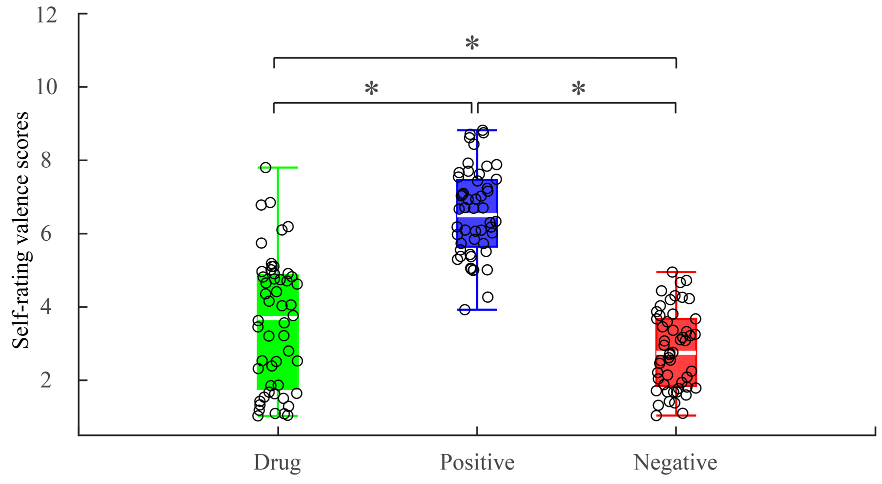

FIGURE 2 | Self-rating valence scores under different experimental conditions. *$p < 0.05$.

PO7 and PO8 within the time window of 180–240 ms, and the averaged LPP at the Cz and CPz electrodes within the time window of 500–1,000 ms. One-way repeated-measures ANOVAs were used to analyze the averaged amplitude of P1, EPN, and LPP with image type (positive, negative, and MA-related) as the experimental condition.

RESULTS

Task 1: Valence Scores

A one-way repeated measures ANOVA showed a main effect of image type [$F_{(2,\ 50)} = 120.436$; $p < 0.001$; $\eta_p{}^2 = 0.828$] on reported valence. *Post hoc* pairwise comparisons indicated valence scores associated with MA-related images ($M = 3.57$, $SD = 1.78$) were significantly higher than those for the negative images [$M = 2.82$, $SD = 1.05$] ($p = 0.004$) and significantly lower than those for the positive images ($M = 6.54$, $SD = 1.18$, $p < 0.001$) (**Figure 2**). Importantly, while MA-related images were rated higher than negative images, the mean value was considerably lower than the median, suggesting MA-related images were emotionally negative stimuli for MA-addicts.

Task 2: Reaction Times

A one-way, repeated-measures ANOVA showed there was a significant main effect of image type [$F_{(2,\ 50)} = 4.635$; $p = 0.014$; $\eta_p{}^2 = 0.156$] on reaction time. *Post hoc* pairwise comparisons indicated reaction times were significantly longer following negative images ($M = 1801.57$, $SD = 401.61$) than positive images ($M = 1657.24$, $SD = 359.04$, $p = 0.036$) and MA-related images ($M = 1676.56$, $SD = 304.66$, $p = 0.030$). There was no significant difference between the reaction time after positive images and MA-related images ($p > 0.99$) (**Figure 3**). This suggests MA-addicts' behavioral responses to drug images

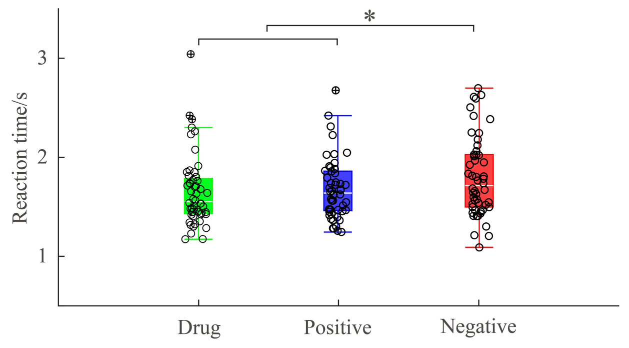

FIGURE 3 | Reaction time under different experimental conditions. $^*p < 0.05$.

were consistent with their behavioral responses to positive emotional images.

Task 2: Electroencephalography Results

P1 Results

One way, repeated measures ANOVA revealed a main effect of image type on the P1 amplitude [$F_{(2, 50)} = 5.425$; $p = 0.007$; $\eta_p{}^2 = 0.178$]. *Post hoc* pairwise comparisons indicated that the P1 amplitudes elicited by MA-related images ($M = 0.90$, $SD = 2.22$) were significantly smaller than those elicited by positive ($M = 1.37$, $SD = 2.43$, $p = 0.049$) or negative ($M = 1.37$, $SD = 2.43$, $p = 0.017$) images. There was no significant difference between P1 amplitudes elicited by positive images and negative images ($p > 0.99$). P1 brain topography illustrated that the P1 component was particularly robust in the occipital-temporal cortex (**Figure 4**). The P1 component has been shown to be closely related to early visual processing (Schupp et al., 2006; Zhang et al., 2014). Thus, this finding could suggest that the early visual processing of MA-related images differed in some way from the early processing of non–drug-related emotional stimuli.

Early Posterior Negativity Results

One-way repeated measures ANOVA showed a significant main effect of image type [$F_{(2, 50)} = 14.303$; $p < 0.001$; $\eta_p{}^2 = 0.364$] on EPN amplitude. *Post hoc* pairwise comparisons indicated that the averaged EPN amplitude evoked by negative images ($M = -0.49$, $SD = 3.17$) was significantly lower than that evoked by MA-related images ($M = -1.32$, $SD = 3.12$, $p < 0.001$) and by positive images ($M = -1.28$, $SD = 3.67$, $p < 0.001$). There was no significant difference between the EPN amplitude evoked by MA-related images and positive images ($p > 0.99$). Brain topography illustrated the EPN was particularly robust in the occipital cortex (**Figure 5**). EPN amplitudes are closely related to the middle stage of specific image content processing (Zhang et al., 2014). Thus, these results indicate brain activity associated with the middle stage of drug-related image processing was indistinguishable from that associated with non–drug-related positive images.

Late Positive Potential Results

A one-way repeated measures ANOVA showed a significant main effect of image type [$F_{(2, 50)} = 10.478$; $p < 0.001$; $\eta_p{}^2 = 0.295$] on LPP amplitude. More specifically, *post hoc* pairwise comparisons indicated that the average LPP amplitude evoked by MA-related images [$M = 1.46$, $SD = 1.51$] was significantly lower than that evoked by positive images ($M = 2.15$, $SD = 1.45$, $p = 0.004$) and by negative images ($M = 2.40$, $SD = 1.50$, $p < 0.001$). There was no significant difference in LPP amplitude between positive images and negative images ($p = 0.513$). Brain topography of the LPP illustrated it was particularly robust in the parietal cortex (**Figure 6**). The LPP amplitude is closely related to the evaluation of emotional stimuli and response preparation (Lang and Bradley, 2010; Yang et al., 2015). Thus, these results indicate that MA addicts may have reverse inhibition in their emotional appraisal and reaction preparation to drug-related stimuli (Moser et al., 2006).

DISCUSSION

The present study investigated behavioral and neural responses to drug-related and non–drug-related emotional stimuli in MA addicts. Previous research has investigated these responses in isolation. The present research represents the first time self-reports have been used in conjunction with reaction times and ERP characteristics to explore this question. We found behavioral and brain response patterns to drug-related stimuli differed from those for processing non–drug-related emotional stimuli. More specifically, participants reported the valence of drug-related images was significantly lower (higher) than positive (negative) stimuli. Moreover, drug-related images corresponded to reaction times that were indistinguishable from the response to positive images, and significantly quicker than the response to negative images. This relationship was mirrored in EPN response amplitudes, with responses to MA-related imagery evoking larger amplitudes than negative imagery, that were indistinguishable from responses to positive stimuli. We also found evidence for reverse inhibition in action preparation and emotional appraisal to drug stimuli in MA-abstinent addicts.

Stimulants such as methamphetamine are characterized by their ability to elicit rapid euphoria. Studies have shown that such drugs are perceived as more arousing and pleasant among people who are drug-dependent than people who are not (Jayanthi et al., 2021). Nevertheless, there is also evidence drug addicts tend to rate drug-related stimuli as negative (Yang et al., 2015). In the present study, although the self-assessment scores on the emotional valence of the MA-related stimuli were significantly higher than those on the negative stimuli, participants gave a negative evaluation to the drug-related stimuli. This negative assessment may be due negative consequences of the drug. For example, negative emotional experiences after the direct effects of the drug has worn off (May et al., 2020), or from punishment by incarceration. Laws and regulations unambiguously define drug taking and trafficking as illegal acts. In turn, individuals are all too aware of the dangers of drug use, perhaps eliciting negative evaluations of them.

Despite negative self-assessments of drug-related stimuli, our behavioral data demonstrates that MA-dependent participants' reaction times after viewing non–drug related negative emotional

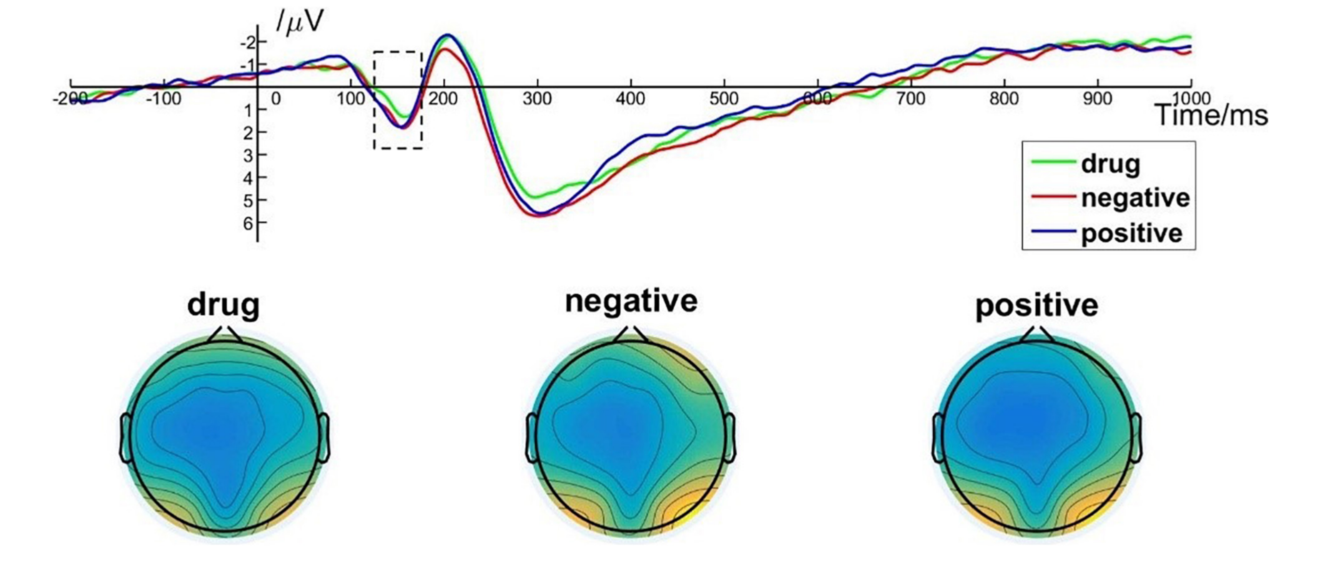

FIGURE 4 | P1 component elicited under different conditions at electrode sites PO7, PO8, O1, and O2 and brain topography of P1.

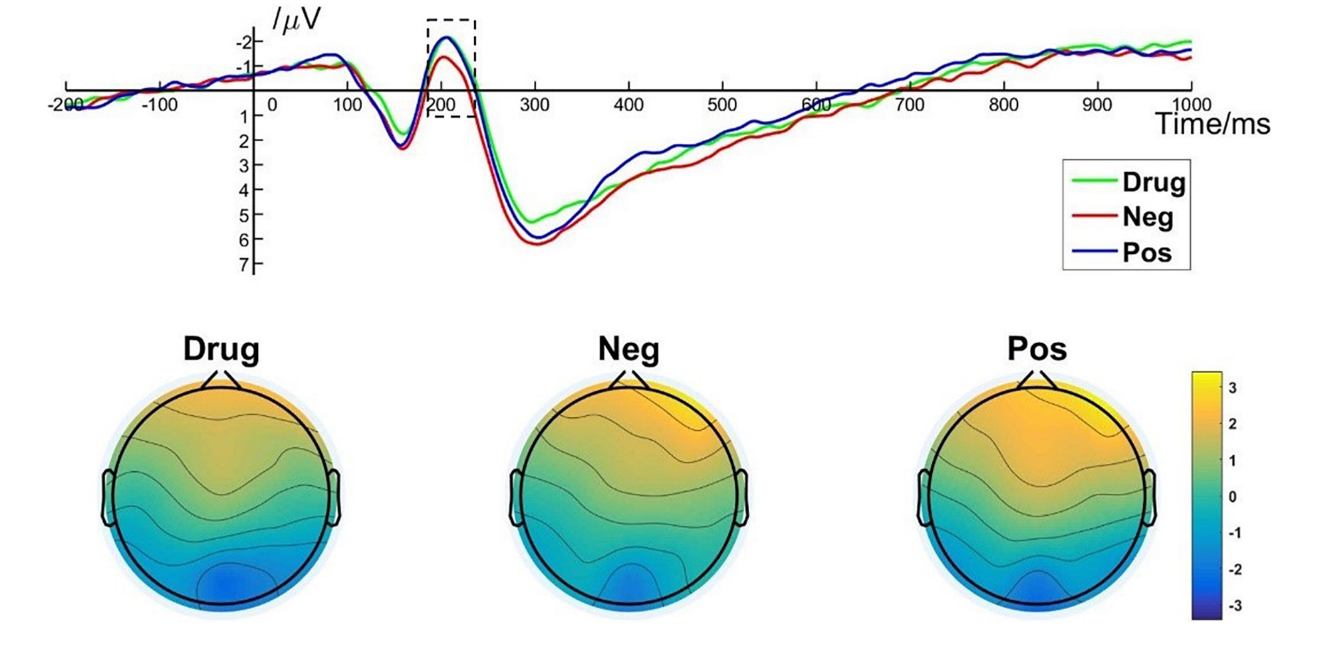

FIGURE 5 | EPN component elicited under different conditions at electrode sites PO7, PO8, and brain topography of EPN.

images were significantly slower than those after viewing MA-related images or non–drug related positive images. By contrast, there was no significant difference between reaction times after viewing MA-related images and non–drug related positive images. This aligns with previous studies which found that performance after viewing negative non–drug related stimuli were significantly slower (Li et al., 2019), whereas performance under positive emotions were significantly improved (Prével et al., 2021). Pereira et al. (2006) used four consecutive behavioral experiments to show that when positive, neutral, or negative emotional images were presented randomly or when similar types of images were presented in groups, the reactions of participants to positive images were significantly faster than their reactions to negative images (Pereira et al., 2006). Li et al. (2019) combined EEG with a cued-action task and found that negative stimuli significantly slowed reaction time, largely due to negative emotional processing consuming more resources than non-emotional processing, with this interference effect mainly occurring in the late action preparation phase (Li et al., 2019).

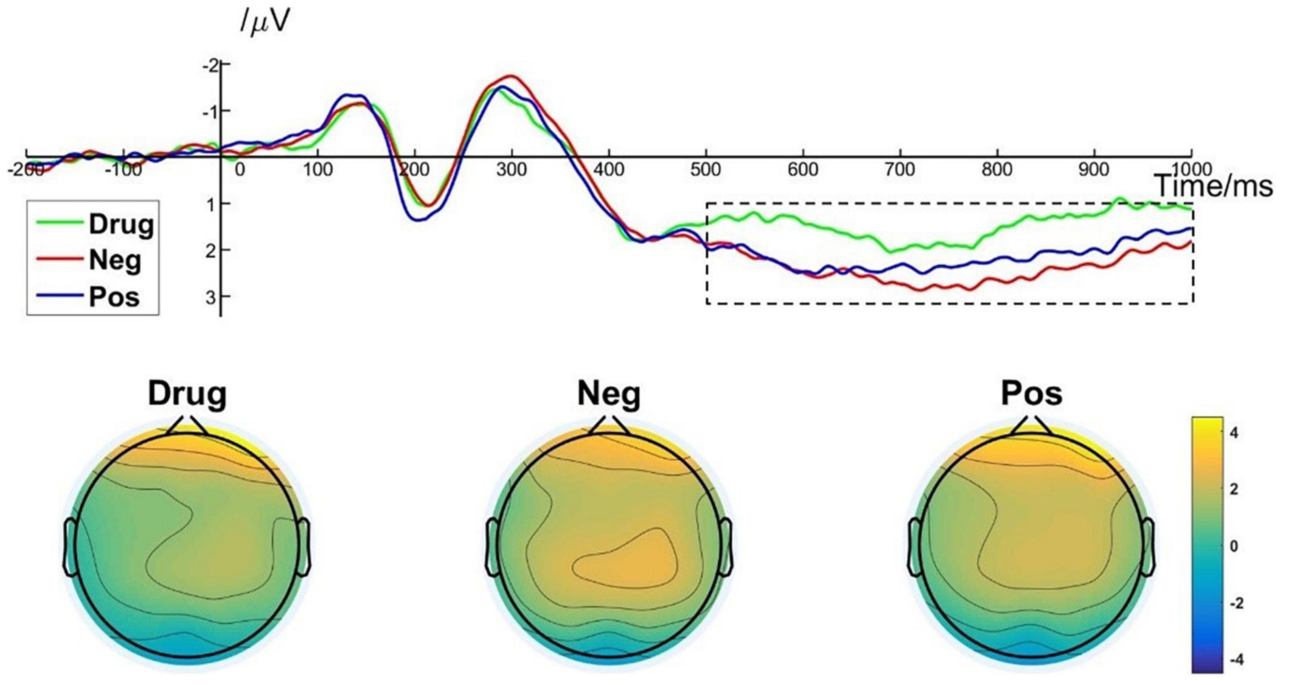

FIGURE 6 | LPP component elicited under different conditions at electrode sites Cz, CPz, and brain topography of LPP.

The present study examined ERP components (P1, EPN, and LPP) that have been found to be sensitive to emotional processing (Lang and Bradley, 2010; Luis, 2014). The P1 component is evoked in the occipital lobe and is associated with attentional resources for early visual processing. Previous studies have observed an enhanced amplitude of the P1 component elicited by drug- or alcohol-related stimuli compared with neutral stimuli in addicts (Kroczek et al., 2018), suggesting they have an attention bias to these stimuli. However, the present results showed that P1 amplitudes elicited by MA-related images were significantly smaller than those elicited by positive or negative images. The present result may be explained by mechanisms underlying the processing of novel stimuli. Based on the existence of a fast magnocellular circuit (Schönwald and Müller, 2014), P1 may reflect the automatic processing of visual stimuli and be related to a rapid extraction of the novel saliency of the information (Piccardi et al., 2020). For addicts, drug-related stimuli may be considered routine and ordinary, whereas emotionally charged images such as fires, car crashes, and beautiful scenery could be construed as more novel. In addition, previous studies have shown that people tend to have a negative stimulus bias. Evidence has shown that relative to neutral stimuli, emotional stimuli elicit larger P1 amplitudes (Rsg et al., 2019). Given we found no difference between P1 amplitudes for positive and negative images, perhaps the circuitry responsible for early emotional processing is impaired in MA addicts.

The occipital-temporal EPN exhibited a more negative deflection for MA-related images and images associated with positive stimuli, than with those elicited in response to negative images. In fact, we detected no significant difference between the EPN elicited by MA-related and positive imagery, indicating that the responses were indistinguishable. The EPN is typically considered an ERP component related to early selective attentional processing and specific content distinctions of emotional stimuli (Weinberg and Hajcak, 2010; Farkas et al., 2020). Schupp et al. (2006) identified the EPN as the first neural activity that reflects the emotional characteristics of a stimulus (Schupp et al., 2006). Some studies have shown that EPNs are larger for emotional stimuli than for neutral stimuli (Lang and Bradley, 2010). Consistent with our results, Francesco et al. (2015) demonstrated that relative to neutral stimuli, emotional stimuli enhanced the EPN over the occipital brain region and that the EPN was more pronounced for positive than for negative stimuli. Moreover, similar to positive stimuli, cigarette-related stimuli elicited a larger EPN than did negative stimuli (Francesco et al., 2015). However, there are also studies showing that heroin-related images elicit a larger EPN than both negative and positive images (Yang et al., 2015). In the present study, the similarity between MA-related and positive imagery elicited EPN amplitudes may suggest that the brain processing pathways for drug-related stimuli partially overlap with the processing pathways for positive emotional stimuli in addicts.

Another signature of the ERP sensitive to emotional processing examined in the present study was the centroparietal LPP, a component thought both to reflect the in-depth evaluation and motivational relevance of emotional stimuli, and be related to response preparation (Lang and Bradley, 2010; Yang et al., 2015; Kaunhoven and Dorjee, 2021). Our results showed that LPPs elicited by MA-related stimuli were significantly smaller than those elicited by negative or positive stimuli, whereas there was no significant difference between positive and negative stimuli. Yang et al. (2015) used an emotional Stroop task to explore differences in emotional processing between addicts and non-addicts. Their LPP results are consist with those in the present study. We speculate that the smaller LPP associated with MA-related stimuli may be closely related to the current situation of the participants in the present study. That is, they may inhibit their motivation for approaching drug-related stimuli because they are in compulsory isolation and are receiving anti-drug education, which may be understood as response inhibition. Moser et al. (2006) found that when participants were asked to actively suppress their responses to negative images of high arousal, there was a decrease in the LPP amplitude (Moser et al., 2006). However, inconsistent with our findings, previous studies have found that the amplitude of the LPP induced by drug-related stimuli is greater than that for general emotional stimuli (Dunning et al., 2011), suggesting that addicts may devote more cognitive resources to drug-related stimuli and that their motivation toward drugs is stronger. In addition, previous studies assessing people without drug addiction have found that the LPP evoked by negative stimuli was significantly larger than that evoked by positive stimuli. From an evolutionary perspective, people would instinctively react stronger to negative stimuli that may threaten them (Quiñones-Camacho et al., 2018). On the contrary, given we found no difference in LPPs evoked by negative and positive stimuli, perhaps chronic methamphetamine abuse damages the neural circuits associated with emotional processing in addicts and reduces their sensitivity to non–drug-related emotional stimuli.

CONCLUSION

In conclusion, at the behavioral level, despite negative self-assessments of drug-related imagery, MA-addicts reacted as quickly to drug-related imagery as they did to positive imagery. At the neural level, we found evidence for increased attentional resource allocated to the middle stage of drug imagery processing. In the late stage of drug imagery processing, MA-addicts showed reduced brain activity associated with drug-related stimuli, suggesting a reverse inhibition in action preparation and emotional appraisal to drugs. These findings may provide a reference for clinicians treating drug-taking behavior and for the development of new models of rehabilitation therapy.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Ethics Committee of Shanghai University of Sport (No. 102772019RT041) and conducted in accordance with this approval. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

XL, CZ, and HW designed and conducted the experiments. XL and YZ contributed to the acquisition of data. GZ, YL, and XL analyzed the data. XL and HW wrote the manuscript. XL and CZ provided critical revision of the manuscript for important intellectual content. All authors critically reviewed content and approved final version for publication.

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SYSTEMATIC REVIEW
published: 24 June 2022
doi: 10.3389/fnhum.2022.891095

Effects of Exercise on Neural Changes in Inhibitory Control: An ALE Meta-Analysis of fMRI Studies

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It is widely known that exercise improves inhibitory control; however, the mechanisms behind the cognitive improvement remain unclear. This study analyzes the extant literature on the neuronal effects of exercise on inhibitory control functions. We searched four online databases (Pubmed, Scopus, PsycINFO, and Web of Science) for relevant peer-reviewed studies to identify eligible studies published before September 1, 2021. Among the 4,090 candidate studies identified, 14 meet the inclusion criteria, and the results of 397 participants in these 14 studies are subsequently analyzed. We quantify the neural effects on the entire brain by using GingerALE software and identify 10 clusters of exercise-induced neuronal with either increases/decreases in the superior temporal gyrus (BA 22), precuneus (BA 7), superior frontal gyrus (BA 10), cuneus (BA 19), precuneus (BA 19), caudate, posterior cingulate (BA 19), middle temporal gyrus (B 37), parahippocampal gyrus (BA 30), precentral gyrus (BA 6). Meta-analytic coactivation map (MACM) showed that multiple functional networks overlap with brain regions with activation likelihood estimation (ALE) results. We propose the effect of exercise on neural activity is related to inhibitory control in the extended frontoparietal, default mode network (DMN), visual network, and other pathways. These results provide preliminary evidence of the neural effects of exercise on inhibitory control.

Keywords: exercise, inhibitory control, meta-analysis, activation likelihood estimation, fMRI

OPEN ACCESS

Edited by:
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Specialty section:
This article was submitted to Cognitive Neuroscience, a section of the journal Frontiers in Human Neuroscience

Received: *07 March 2022*
Accepted: *08 June 2022*
Published: *24 June 2022*

Citation:
Wu J, Xiao W, Yip J, Peng L, Zheng K, Takyi Bentil O and Ren Z (2022) Effects of Exercise on Neural Changes in Inhibitory Control: An ALE Meta-Analysis of fMRI Studies. Front. Hum. Neurosci. 16:891095. doi: 10.3389/fnhum.2022.891095

INTRODUCTION

Inhibitory control or inhibition is defined as suppressing prepotent responses to goal-irrelevant stimuli and contributes to anticipation, planning, and goal setting. Inhibitory control is one of the three core executive functions of the brain (Aron, 2007; Liang et al., 2021b). People who suffer from impaired inhibitory control have a lower quality of life and develop health problems and diseases which applies to healthy and sick people (Liang et al., 2021a). Meanwhile, impaired inhibitory control could be a hallmark feature of several neuropsychological DSM-5 disorders including attention-deficit/hyperactivity disorder (ADHD; Crosbie et al., 2008; Bari and Robbins, 2013), bipolar disorder (Hidiroglu et al., 2015), schizophrenia (Enticott et al., 2008; Hughes et al., 2012), and substance use disorders (Liao et al., 2014; Lee et al., 2015). Although the disorders listed here are primarily characterized by difficulties in controlling behavior (Brady et al., 2011; Sofuoglu et al., 2013; Baumeister et al., 2018), they are also found in normal cognitive aging

(Coxon et al., 2012; Smittenaar et al., 2015). Thus, to understand the risk of developing these disorders and contribute to current prevention and treatment measures, an analysis of the neural underpinnings of inhibitory control is essential and timely.

Physical activity has garnered significant attention as a potentially effective method for elevating cognitive function and improving brain health throughout life (Loprinzi et al., 2013; Ji et al., 2021). Meta-analyses of healthy participants (Li et al., 2020; Amatriain-Fernandez et al., 2021; Chen et al., 2021), autism spectrum disorder (ASD; Liang et al., 2021b), mild cognitive impairment (MCI; Biazus-Sehn et al., 2020) as well as ADHD patients (Liang et al., 2021a) have shown that exercise has a positive effect on inhibitory control in individuals. Neuroimaging studies have also demonstrated the inhibitory control mechanisms of the brain by exploring the relationship between exercise and brain region activation during specific tasks (e.g., flanker, go/no-go, and Stroop tasks). Previous studies reported that the "cognitive control network" actively coordinates multiple brain regions, such as the frontal cortex (including the anterior cingulate cortex), parietal cortex, motor regions, and cerebellum (Niendam et al., 2012; Akatsuka et al., 2015; Chu et al., 2015). The effects of exercise on functional changes in inhibitory control are not apparent. Indeed, some studies report an increase in the activation of the prefrontal and parietal lobes following exercise intervention (Mehren et al., 2019c), whereas others reported less activation in the frontal and temporal lobes during similar inhibitory-based tasks (Krafft et al., 2014; Hsu et al., 2018).

The last few years have seen the introduction of several tools for performing a meta-analysis of data obtained from brain imaging research, allowing for the quantitative integration of findings from different studies. Activation likelihood estimation (ALE) is a relatively way to estimate the probability that at least one activation focus from a set of experiments lies at the location of a specific voxel, using Gaussian assumptions of spatial uncertainty (Turkeltaub et al., 2002) This study, using the ALE method, aimed to explore the overall neural changes in inhibitory control associated with exercise. We hypothesized the critical regions of exercise-induced inhibitory control are related to several frontal and parietal cortex brain areas. To validate ALE results whether overlap the brain networks to related frontoparietal or other brain networks, we applied a meta-analytic co-activation model (MACM) approach using activation clusters as regions of interest (ROIs) from our ALE results.

METHOD

The meta-analysis in this study is completed and reported by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Statement (PRISMA). The protocol was registered as trial registration number CRD42021285736 under the International Prospective Register of Systematic Reviews (PROSPERO).

Search Strategy

Four electronic databases (Pubmed, Scopus, PsycINFO, and Web of Science) were searched from their inception to September 1, 2021, to identify all published studies on functional magnetic resonance imaging (fMRI) that investigate the impact of exercise on the activation of different brain areas during inhibitory control tasks. The initial search used three key terms: physical activity or exercise, inhibitory control, and fMRI. We also hand-searched recent systematic reviews and meta-analyses to identify potential studies (Liang et al., 2021a; Yu et al., 2021). The search was limited to English-language results and human subjects. The reference lists of included studies were manually reviewed for relevant articles that were captured through the database searches. The detailed keyword search strategy is presented in the **Appendix Table**.

Study Selection

The screening for relevant studies was conducted in accordance with the PICOS (participants, intervention, comparisons, outcomes, and study design) principles. The participants included individuals of all ages and pathologies. The studies must have investigated the effect of exercise on inhibitory control and examined pre/post-intervention with at least one group assigned to physical activity/exercise intervention. During fMRI scanning, studies must have assessed brain activation patterns *via* completed inhibitory control tasks (e.g., go/no-go, stroop, flanker, or Simon tasks). For inclusion, retrievable data in standard Talairach or Montreal Neurologic Institute (MNI) space was also required. Finally, the chosen studies included randomized controlled trials (RCTs) and non-randomized controlled trial studies (NRCTs) published in peer-reviewed journals.

Two reviewers independently conducted the multi-step search process based on these selection criteria and screened the studies based on their title and abstract. Full-length texts were eventually used to identify eligible articles. If consensus could not be reached, a third reviewer made the final decision after discussion with the two reviewers.

Data Extraction

A standardized data extraction form was developed to extract relevant data from each study, including the bibliographic details (author and year), participant characteristics (sample size, sex, and age range), intervention components (intervention design and duration), fMRI task, software used, and active results/foci.

Quality Assessment

The Physiotherapy Evidence Database (PEDro) scale, a reliable and valid instrument for assessing the methodological quality of studies that focus on the effects of physical activity on cognitive functions, was used to determine the methodological quality (Sherrington et al., 2000). This scale includes 11 rating criteria including eligibility, randomization, allocation, blinding (subjects and experimenter), intention-to-treat, between-group comparison, and point measures. The methodological criteria were scored as Yes (one point), No (zero points) or Do not know (zero points). The PEDro score of each selected study served as an indicator of the methodological quality (<4 = poor; 4–5 = fair; 6–8 = good; and 9–10 = excellent).

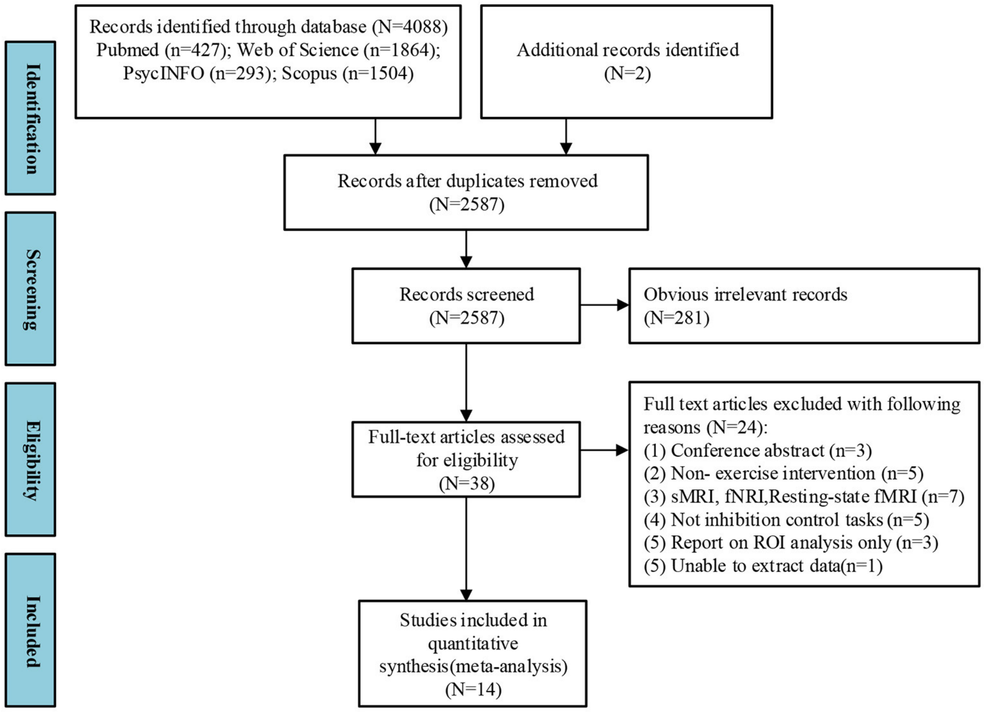


FIGURE 1 | PRISMA flow diagram of selected studies. Multi-step search process shows the number of studies screened and those that meet the inclusion criteria.

The fMRI quality was determined from a set of guidelines for the standardized reporting of the fMRI studies and used to assess the fMRI study design/reporting quality and quality of the fMRI data of each included study (Poldrack et al., 2008). The fMRI form has 8-item rating criteria for eligibility, the experimental design, handedness and gender of participants, explanation for rejected data, details of the imaging parameters, software analysis method and package used, motion correction method during pre-processing, multiple comparison correction, and detailed description of the first and second level analyses.

Data Analysis

The ALE is a reliable quantitative method for coordinate-based meta-analyses to identify brain activation during cognitive functions after exercise (Laird et al., 2005). In this study, GingerALE v2.3.6 (http://www.brainmap.org) software is used to analyze the data. A statistical threshold of uncorrected $p < 0.001$ and a minimum cluster size of 100 mm^3 were used (Meng et al., 2020). The ALE maps were imported into Mango Version 4.1 (http://ric.uthscsa.edu/mango/mango.html) software and overlaid on an anatomical template in MNI space for visualization. The effect of exercise on behavioral performance is not examined due to missing data and changes in an inhibitory control task that resulted in the effect magnitude being inestimable.

Additionally, to obtain the MACM based on the ALE results, we followed the procedure proposed by Robinson et al. (2010) as implemented in NeuroSynth (http://neurosynth.org/; Yarkoni et al., 2011). The activation clusters as seed ROIs were separately entered into NeuroSynth to evaluate the MACM. In brief, the software searches among more than 11,000 fMRI studies (totaling 413,429 activations in the MNI152 coordinate space) those reporting activation in a spherical seed (6 mm) around the searched coordinates. The identified co-activations are then pooled together to form the MACM output that is corrected for multiple comparisons ($p < 0.01$ false discovery rate; FDR as provided in NeuroSynth). Namely, a z-score is assigned to each voxel, representing the strength of the association between a given voxel and the seed coordinates.

RESULTS

Study Selection

Four thousand and eighty-eight studies were identified from the four databases, and two studies were identified from other systemic reviews. Included studies were chosen after thoroughly screening the titles, abstracts, and full text. Fourteen studies were identified for the meta-analysis (**Figure 1**).

Study Characteristics

Table 1 lists the characteristics of the 14 studies that involved 397 participants. Six studies (Mehren et al., 2019a,b,c; Won et al., 2019; Cui et al., 2020; Meng et al., 2020) utilized acute exercise paradigms and eight studies (Colcombe et al., 2004; Liu-Ambrose et al., 2012; Krafft et al., 2014; Sachs et al., 2017; Hsu et al., 2018;

TABLE 1 | Descriptive characteristics of included studies.

References	Design	Participants	Sample male/ female	Age (years old)	Intervention for exercise group	Duration	fMRI task	Software	Active Results/Foci
Colcombe et al. (2004)	RCT	Older adults	M: 11 F: 18	65.6 ± 5.66	Walking	40–45 min/session * 3 days/week * 6 months	Flanker task	SPM99	Pre>Post/ 0 Post>Pre/ 3
Liu-Ambrose et al. (2012)	RCT	Senior women	F: 52	Rt1:69.7 ± 2.8 Re2:68.9 ± 3.2 Bat: 69.3 ± 3.0	Resistance exercise	Rt1:1 days/week *52 months Re2:2 days/week *52 months Bat: 2 days/week *52 months	Eriksen flanker task	FEAT and FSL	Pre>Post/ 0 Post>Pre/ 12
Krafft et al. (2014)	RCT	Overweight children	M: 7 F: 17	9.7 ± 0.8	Tag and jump rope	405 min/session * 7 days/week * 8 months	Flanker task	AFNI	Pre>Post/ 6 Post>Pre/ 4
Metcalfe et al. (2016)	nRCT	Adolescents with bipolar disorder	M: 13 F: 17	16.8 ± 1.4	Recumbent bicycle-ergometer	27 min	Go-no-go task	FSL	Pre>Post/ 5 Post>Pre/ 3
Sachs et al. (2017)	nRCT	Children	M: 5 F: 8	8.85	Soccer and swimming	60 min/session * 2 or 3 days/week * 5 years	Color-word stoop task	FSL	Pre>Post/ 1 Post>Pre/ 0
Martinsen et al. (2018)	nRCT	Fibromyalgia	F: 19	49.6	Resistance exercise	60 min/session * 2 days/week * 15 weeks	Color-word stoop task	SPM8	Pre>Post/ 0 Post>Pre/ 3
Hsu et al. (2018)	RCT	SIVCI	M: 4 F: 6	M:71.1 ± 8.8 F: 73.5 ± 7.9	Walking	60 min/session * 3 days/week * 6 months	Flanker task	FSL	Pre>Post/ 16 Post>Pre/ 0
Pensel et al. (2018)	nRCT	Order adults	M:23	M:49.00 ± 5.32	Running	60 min/session * 3 days/week * 6 months	Flanker task	SPM8	Pre>Post/ 0 Post>Pre/ 22
Wu et al. (2018)	RCT	Order adults	16	64.9 ± 2.8	Taichi	60 min/session * 3 days/week * 12 weeks	Stoop task	SPM12	Pre>Post/ 0 Post>Pre/ 5
Mehren et al. (2019a)	nRCT	Adults	MI:M:16 F:16 HI:M:15 F:16	MPA:29.3 ± 8.5 MVPA:28.6 ± 7.7	Cycling and Hiit	30 min	Go-no-go task	SPM12	Pre>Post/ 0 Post>Pre /5
Mehren et al. (2019c)	nRCT	Adult patients with ADHD	M: 20 F: 3	31.4 ± 9.6	Cycling	30 min	Go-no-go task	SPM12	Pre>Post/ 0 Post>Pre/ 3
Mehren et al. (2019b)	nRCT	Adult patients with ADHD	M: 16 F: 4	29.9 ± 9.5	Cycling	30 min	Flanker task	SPM12	Pre>Post/ 0 Post>Pre/ 5
Won et al. (2019)	nRCT	Older adults	M: 8 F: 24	66.2 ± 7.3	Cycling	30 min	Eriksen flanker task	AFNI	Pre>Post/ 2 Post>Pre/ 9
Cui et al. (2020)	nRCT	Female college students	F: 43	HF:20.32 ± 0.75 LH:20.35 ± 0.61	Cycling	30 min	Stoop task	SPM23	Pre>Post/ 0 Post>Pre/ 10

RCT, randomized control trial; nRCT, non-randomized control trial; SIVCI, subcortical ischemic vascular cognitive impairment; ADHD, attention deficit hyperactivity disorder; BAT, twice-weekly balance and tone training; RT1, once-weekly resistance training; RT2, twice-weekly resistance training; HT, high-fit group; LF, low-fit group; MI, moderate intensity; HI, high intensity; HITT, high-intensity interval training.

TABLE 2 | Methodological quality assessment of included studies.

References	Eligibility criteria	Random allocation	Concealed allocation	Similar at baseline	Subject blinded	Therapist blinded	Assessor blinded	Dropout	Intention-to-treat analysis	Between-group comparison	Points measures	Total score	Overall study quality
Colcombe et al. (2004)	0	0	0	1	0	0	0	1	1	1	1	5	Good
Liu-Ambrose et al. (2012)	1	1	1	1	0	0	1	1	1	1	1	9	Excellent
Krafft et al. (2014)	1	1	1	1	0	0	0	1	1	1	1	8	Good
Metcalfe et al. (2016)	1	0	0	1	0	0	0	1	1	1	1	6	Good
Sachs et al. (2017)	1	0	0	1	0	0	0	1	1	1	1	6	Good
Martinsen et al. (2018)	1	0	0	1	0	0	0	1	1	1	1	6	Good
Hsu et al. (2018)	1	1	1	1	0	0	0	1	1	1	1	8	Good
Pensel et al. (2018)	1	0	0	1	0	0	0	1	1	1	1	6	Good
Wu et al. (2018)	1	1	0	1	0	0	1	1	1	1	1	8	Good
Mehren et al. (2019a)	1	0	0	1	0	0	0	1	1	1	1	6	Good
Mehren et al. (2019c)	1	0	0	1	0	0	0	1	1	1	1	6	Good
Mehren et al. (2019b)	1	0	0	1	0	0	0	1	1	1	1	6	Good
Won et al. (2019)	1	0	0	1	0	0	0	1	1	1	1	6	Good
Cui et al. (2020)	1	1	1	1	0	0	0	1	1	1	1	8	Good

Yes = 1; No or Do not know = 0.

TABLE 3 | fMRI quality assessment of included studies.

References	fMRI design	Sample handedness reported	Sample gender reported	Scan rejection mentioned	Scan rejection reason	Volume acquired per session	Software package specified	Method for motion correction described	Method for multiple comparison correction described	Type of correction applied	First level contrasts described	Second level contrasts described
Colcombe et al. (2004)	1	0	0	0	0	0	0	0	0	Voxel wise	0	1
Liu-Ambrose et al. (2012)	1	1	1	0	0	0	1	1	0	Cluster	1	1
Krafft et al. (2014)	1	1	1	1	0	0	1	0	1	Cluster	0	0
Metcalfe et al. (2016)	1	0	1	0	0	0	1	1	0	Unclear	1	0
Sachs et al. (2017)	1	1	1	0	0	0	1	1	0	Cluster	0	0
Martinsen et al. (2018)	1	0	1	0	0	0	1	0	1	Unclear	1	1
Hsu et al. (2018)	1	0	1	0	0	0	1	1	0	Cluster	0	1
Pensel et al. (2018)	1	1	1	0	0	0	1	0	1	Voxel wise	1	1
Wu et al. (2018)	1	1	1	0	0	0	1	1	1	Voxel wise	1	1
Mehren et al. (2019a)	1	1	1	0	0	0	1	0	1	Voxel wise	0	0
Mehren et al. (2019c)	1	1	0	0	0	0	1	0	1	Voxel wise	0	0
Mehren et al. (2019b)	1	1	1	0	0	0	1	0	1	Voxel wise	0	0
Won et al. (2019)	1	1	1	0	0	0	1	1	0	Voxel wise	0	0
Cui et al. (2020)	1	1	1	0	0	0	1	1	1	Voxel wise	1	1

Yes = 1; No or do not know = 0.

TABLE 4 | ALE clusters derived from inhibitory control task in overall analysis.

Cluster	Region	Brodmann area	x	y	z	ALE extrema	*p*
Activation increases							
1	L Superior temporal gyrus	BA 22	−56	−32	4	0.015	<0.001
2	R Precuneus	BA 7	32	−66	44	0.012	<0.001
3	R Superior frontal gyrus	BA 10	27	60	20	0.012	<0.001
4	R Cuneus	BA 19	34	82	34	0.010	<0.001
5	R Precuneus	BA 19	32	−76	36	0.009	<0.001
Activation decreases							
1	R Caudate	–	40	−40	4	0.009	<0.001
2	R Posterior cingulate	B31	16	−64	18	0.009	<0.001
3	R Middle temporal gyrus	BA 37	48	−60	−2	0.008	<0.001
4	L Parahippocampal gyrus	BA 30	−10	−44	−2	0.008	<0.001
5	R Precentral gyrus	BA 6	60	6	28	0.008	<0.001

R, right; L, left.

Martinsen et al., 2018; Pensel et al., 2018; Wu et al., 2018) utilized chronic exercise routines. Three neurocognitive tasks (including flanker, stroop, and go/no-go tasks) were used to assess inhibitory control in participants across the studies.

Quality Assessment

Table 2 shows the methodological quality of the studies using the PEDro scale. The total scores range from 6 to 9 ($M = 6.71$). Notably, none of the studies reported blinded data due to the difficulties of using blinded subjects, therapists, and assessors in an exercise intervention. The studies that failed to obtain points in other criteria due to their study design include lack of eligibility ($n = 1$), random allocation ($n = 9$), and concealed allocation ($n = 10$).

Table 3 shows the fMRI quality assessment for all of the studies from a set of guidelines for the standardized reporting of fMRI studies. Other criteria were lacking in at least one reporting guideline, particularly in the scan rejection mentioned ($n = 13$), scan rejection reason ($n = 14$), the method for motion correction ($n = 7$), volume acquired per session ($n = 14$), and clear descriptions of the first ($n = 8$) and second level contrasts ($n = 7$).

The Overall Analysis of Activity Results

Among the 14 studies that assessed brain activation during inhibitory control tasks after exercise, the exercise groups (EGs) show increased brain activation compared to the control groups (CGs) in six clusters: (1) superior temporal gyrus (BA 22), (2) precuneus (BA 7 and BA 19), (3) superior frontal gyrus (BA 10), and (4) cuneus (BA 19). Five regions showed reduced brain activation: (1) caudate gray matter, (2) posterior cingulate cortex (BA 31), (3) middle temporal gyrus (BA 37), (4) parahippocampal gyrus, and (5) precentral gyrus (BA 6), as shown in **Table 4** and **Figure 2**.

Coactivation Maps

Coactivation maps were plotted after the MACM analysis, as shown the **Table 5**. To understand the correspondence between the obtained coactivation maps and the brain functional connectivity networks, we compared it with the cortical parcellation atlas built by Yeo et al. (2011) on 1,000 healthy young subjects. We found that multiple functional networks, including the frontoparietal network, visual network, default mode network, and attention network, overlap with brain regions with ALE results, although this is a subjective judgment.

DISCUSSION

The primary aim of the ALE meta-analysis in this study is to offer the first quantitative summary of the effect of exercise on increased and decreased neural activity of different brain areas during inhibitory control tasks. We identified five clusters of increased neural activity [left superior temporal gyrus, right precuneus (BA 7 and BA 19), right superior frontal gyrus, and right cuneus] and five clusters of diminished neural activity (left parahippocampal, right posterior cingulate, right middle temporal and right precentral gyrus, and right caudate) following exercise. MACM analysis suggested that inhibitory control involved multiple functional networks. These findings may help identify the underlying mechanisms of increased inhibitory control that are exercise-induced.

Previous work found that the neurophysiological mechanism that controls movement is located in the prefrontal cortex (Niendam et al., 2012; Ardila et al., 2018). Our finding shows that there are changes in brain activity in the superior frontal and precentral gyrus of the frontal lobe. It should be noted that both of these regions are responsible for motor control (Niendam et al., 2012; Ardila et al., 2018).

The superior frontal gyrus is also part of the prefrontal cortex, which is responsible for cognitive control functions. This is closely connected with high-level cognitive functions such as interference inhibition, conflict solving, and selective attention (Cabeza and Nyberg, 2000; Baym et al., 2008). The precentral gyrus is part of the supplementary motor area (SMA), which is essential for cognitive control as found in previous studies of concern, especially when motor movements need to be inhibited (Nachev et al., 2008; Aron, 2010).

Our findings showed one change in brain activity in the parietal lobe is the precuneus. The precuneus region is an essential area for attention selection and response to conflict (Indovina and Macaluso, 2004). Previous research found that it plays a pivotal role in the prefrontal-parietal circuit when performing inhibitory tasks (Garavan et al., 2002; Mehren et al., 2019c). Thus, this study concludes that exercise is closely related to connectivity in the frontoparietal network. However, more studies are needed to verify this conclusion.

Besides, the finding showed that three regions' activity changed, including the superior temporal gyrus, middle temporal gyrus, and caudate in the temporal lobe during inhibitory control tasks. It is worthy to note that the superior temporal sulcus typically provides the amygdala with visual information

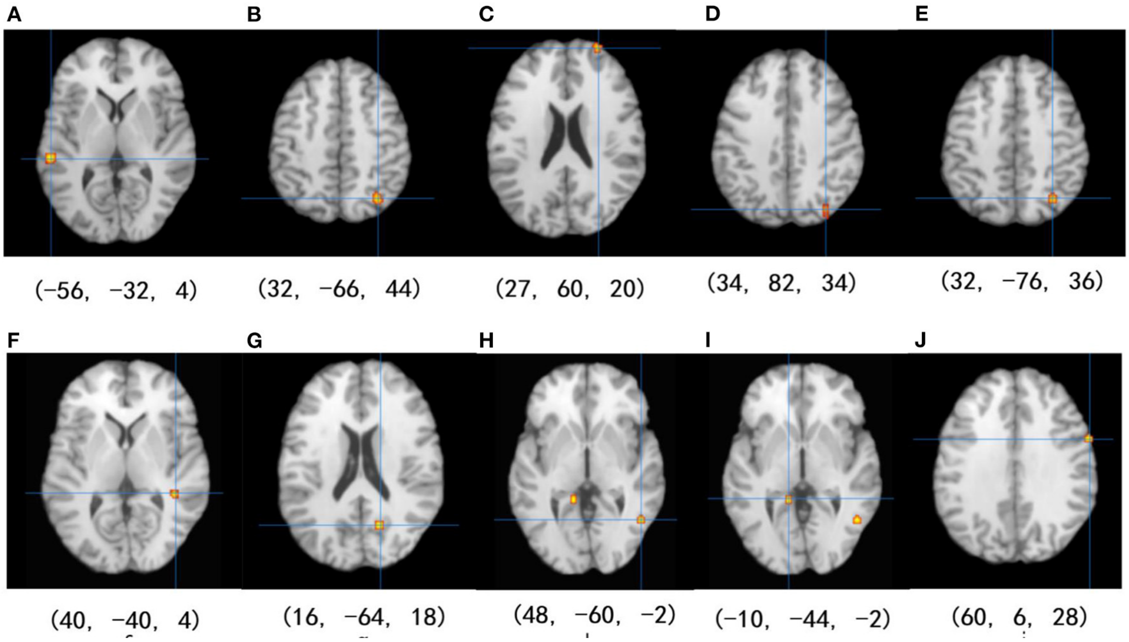


FIGURE 2 | Results of the ALE meta-analysis show increased and reduced activation for inhibitory control in the EGs compared with CGs. Uncorrected $p < 0.001$ and cluster size >100 mm^3 (from **A–D**: activation is increased, and from **E–J**: activation is decreased).

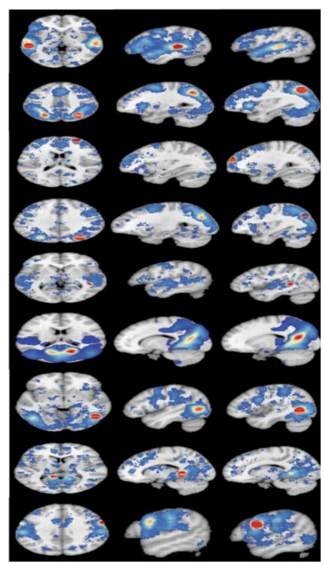
that contributes to identifying the affective or motivational significance of visually perceived objects (Arzimanoglou et al., 2005). An aerobic intervention experiment by Hsu et al. (2018) showed that aerobic intervention alters the activation of the superior temporal gyrus in patients with cognitive impairment and pointed out that there is an apparent correlation between the activation of the superior temporal gyrus and the reaction speed in the go/no-go task. Liu-Ambrose et al. found that after 52 elderly subjects received resistance training twice a week for 12 months, the pathway extending from the left anterior middle temporal gyrus and the left anterior insula to the lateral orbitofrontal cortex was activated during the flanker task (Liu-Ambrose et al., 2012).

It has been proven that the caudate is one of the primary input nuclei receiving inputs from the prefrontal cortex and transferring information to the basal ganglia (Kunishio and Haber, 1994; Haber et al., 2000; Nakahara et al., 2002). The dorsolateral prefrontal cortex-caudate circuit was also shown to be involved in proactive inhibition *via* the indirect pathway (Jahfari et al., 2011). We speculate that exercise effectively activates these pathways in response to inhibitory tasks. However, additional experiments are required for verification.

Finally, we found posterior cingulate gyrus and parahippocampal gyrus have activation changes, and these two regions both belong to the limbic structures. The posterior cingulate gyrus is close to the limbic system and belongs to the cortical region functioning as a gateway between the limbic system and the midbrain and diencephalon (Li et al., 2017). Since the posterior cingulate gyrus and precuneus are identified

TABLE 5 | The results of co-activation maps.

Cluster	x	y	z	L	R
L Superior temporal gyrus	−56	−32	4		
R Precuneus	32	−66	44		
R Superior frontal gyrus	27	60	20		
R Precuneus	32	−76	36		
R Caudate	40	−40	4		
R Posterior cingulate	16	−64	18		
R Middle temporal gyrus	48	−60	−2		
L Parahippocampal gyrus	−10	−44	−2		
R Precentral gyrus	60	6	28		



R, right; L, left.

here, we hypothesize that exhibited hyper-connectivity (i.e., stronger positive connectivity) is shown in the default mode network (DMN) regions during inhibitory control tasks which is consistent with findings in previous studies (Yu et al., 2021). Furthermore, the degree of coupling between the DMN and the frontal-parietal network positively correlates with overall cognitive function. Therefore, the DMN, which is the main component for the stop signal in inhibitory tasks is particularly significant for the impact of physical exercise on inhibitory control ability.

The parahippocampal gyrus is an active region in the limbic system, and exercise intervention appears to strengthen their neuronal excitability, increase the volume of white matter/gray matter, and positively change the production of brain-derived neural factors (Li et al., 2017; Loprinzi, 2017; Muller et al., 2017; Ji et al., 2021). Previous research has validated the effect of exercise on the plasticity of the parahippocampal gyrus, which plays a crucial role in maintaining memory function and aids in spatial information processing and object recognition (Brown and Aggleton, 2001; Raslau et al., 2015). We guess that the parahippocampal gyrus of spatial information processing and object recognition functions are also likely the underlying reason(s) that exercise improves cognitive control function.

There are some limitations to this study. First, only 14 studies are included, which is a smaller sample size. As a result, a subgroup analysis of the exercise intensity and type of exercise is challenging. Second, this study contains different inhibitory control tasks; although the flanker, go-no-go, and stroop tasks are all standard tasks for measuring inhibitory control, the components are slightly different.

CONCLUSIONS

Neural mechanisms increase exercise-induced inhibitory control by changing the activation of single and multiple brain regions. We guess that critical areas mediate inhibitory control and are associated with the frontoparietal, visual network, DMN, and other pathways. However, due to the lenient threshold used in the ALE analysis, further research with more rigorous methods is required to link exercise to neuroplasticity changes with respect to inhibitory control.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

AUTHOR CONTRIBUTIONS

JW and ZR were responsible for the conceptualization, investigation, and hypothesis of the research. JW and WX conducted systematic search, data extraction, quality assessment, and data analyses. JY, KZ, LP, OT, and ZR reviewed and edited the initial draft and revisions. All authors contributed to the article and approved the submitted version.

FUNDING

The article was supported by Research Foundation for Young Teacher of Shenzhen University [grant number QNJS0274]; High-level Scientific Research Foundation for the Introduction of Talent of Shenzhen University [grant number RC00228]; and Natural Science Featured Innovation Projects in Ordinary Universities in Guangdong Province [grant number 2021KTSCX297].

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fnhum.2022.891095/full#supplementary-material

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Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

ORIGINAL RESEARCH
published: 12 July 2022
doi: 10.3389/fnhum.2022.848230

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Relationship Between Gross Motor Skills and Inhibitory Control in Preschool Children: A Pilot Study

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Purpose: Gross motor skills (GMS) and inhibitory control (IC) which are both development in preschool stage is significant for preschooler to healthy growth. However, the evidence of relationship between them in preschoolers are still insufficient, most of studies only focus on youth. Thus, the aim of this research is to examine the association between GMS and IC in preschool children.

Methods: This cross-sectional study used baseline data from a previous intervention study of preschoolers conducted in 2018. GMS were assessed by using the Test for Gross Motor Development (2nd edition) in preschoolers, which includes two subtests of locomotor and object control skills. Total GMS is calculated from the sum of these two subtests. The Fish Flanker task was used to evaluate both accuracy and reaction time of IC. Multivariate linear regression models were established to analyze the relationships between GMS and IC.

Results: A total of 123 preschool-age children (55 girls, 68 boys) were included in the final analysis. After adjusting for confounders, GMS (β = −8.27 ms, 95%CI: −14.2, −2.34), locomotor (β = −11.2 ms, 95%CI: −21.43, −0.97), and object control skills (β = −12.15 ms, 95%CI: −22.07, −2.23) were all negatively related with reaction time of IC.

Conclusion: There was a significant negative correlation between gross motor skills and the reaction time of inhibitory control in preschool children. Further research is needed to verify this finding in prospective and experimental studies.

Keywords: gross motor skills, locomotor skills, object control skills, inhibitory control, preschool children

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Specialty section:
This article was submitted to Cognitive Neuroscience, a section of the journal Frontiers in Human Neuroscience

Received: *04 January 2022*
Accepted: *16 June 2022*
Published: *12 July 2022*

Citation:
Liu J, Li Y, Zhou T, Lu Y, Sang M, Li L, Fang C, Hu W, Sun X, Quan M and Liu J (2022) Relationship Between Gross Motor Skills and Inhibitory Control in Preschool Children: A Pilot Study. Front. Hum. Neurosci. 16:848230. doi: 10.3389/fnhum.2022.848230

Abbreviations: EF, executive function; GMS, gross motor skill; IC, inhibitory control; LS, locomotor skills; OCS, object control skills; IC-ACC, the accuracy of inhibitory control; IC-RT, the reaction time of inhibitory control; TGMD-2, the Test for Gross Motor Development – 2nd edition; BMI, body mass index.

INTRODUCTION

Executive functions (EF) are typically used to describe several top-down higher-order cognitive processes in the prefrontal cortex of the brain that include working memory, cognitive flexibility, and inhibitory control (Diamond, 2013). Collectively, these processes are important in one's ability to plan, focus attention, remember, and juggle multiple tasks. Inhibitory control (IC) is an important role of executive function in young children as it relates to suppressing impulses, inappropriate behaviors, and dismissing goal-irrelevant stimuli in order to achieve desired goals (Brocki and Bohlin, 2004; Tiego et al., 2018). IC is divided into two subdomain Response Inhibition (the ability to inhibit one's impulses to motor response) and Attentional Inhibition, also named interference inhibition (the ability to resist interference from unrelated stimuli) (Tiego et al., 2018). These subdomains often collective referred to as IC. A series of tasks have been used to measure IC in the past, such as Go/No-go, Stop-signal tasks, and Flanker task. Compared with other tasks, Flanker task is more suitable for preschoolers to understand and operate (Mcdermott et al., 2007). IC is important for preschool children, as it reflects their readiness to learn and adapt to complex situations. Preschoolers who fail to develop age-appropriate executive functions can present with low IC. Low IC is often reflected in children with attention deficit hyperactivity disorders (Thorell et al., 2009), difficulties in inhibiting their impulses by responding or reacting immediately to stimuli, an inability to express their thoughts easily (Diamond, 2016), a reduced attention span (Bocharov et al., 2021), and delayed motor development (i.e., a late transition from crawling to walking) (Mohd Nordin et al., 2021). IC also may be related in overeating and obesity (Batterink et al., 2010). Consequently, the promotion of safe and effective IC development activities in preschool children is of significance for their development and progress in educational pursuits.

Motor skills reflect the integration of a series of movements, gross motor skills (GMS) are one of primary parts of motor skills. GMS refers the large, force-producing muscles of limbs and the torso used to achieve a motor goal or task (Clark and Humphrey, 1994). GMS is developed in early life and are the building blocks for later complex motor skills (Barnett et al., 2016). GMS subtests include locomotor skills (LS; e.g., run, jump) and object control skills (OCS; e.g., kick a ball, catch a ball). These subtests are used to transport the body from one site to another and to project or receive objects, especially balls (Ulrich and Sanford, 2000). Evidence has shown that GMS is associated with physical activity and health-related physical fitness and that the development of GMS influences physical health status and motor performance across the lifespan from childhood into adulthood (Lubans et al., 2010).

The relationship between motor skills and executive functions originates from Piaget's 1953 theory of cognitive development which posits the development of motor skills is influenced by a child's interaction with their environment, thereby facilitating children's cognitive development (Piaget and Cook, 1953). This view is supported by the 1993 research of Bushnell and Boudreau (1993) who further proposed that motor development is a prerequisite process for gaining and practicing other cognitive abilities, such as visual depth perception and haptic perception. Neuroimaging studies have shown that the association between GMS and IC is related to the co-activation of the cerebellum and the prefrontal cortex (Berman et al., 1995). Applied research has shown indirect associations between GMS and IC in developmental disorders, such as attention deficit hyperactivity disorders (Kaiser et al., 2015) and developmental coordination disorders (Rigoli et al., 2012). Several studies have investigated the associations between GMS and IC in children and/or adolescents (Roebers and Kauer, 2009; Geertsen et al., 2016), with primary interest in children with disabilities (Hartman et al., 2010; Michel et al., 2011; Schott and Holfelder, 2015). Meanwhile, in a systematic review of the associations between motor skills and cognitive function, including IC, in healthy children ages 4–16 years, Van der Fels et al. (2015) found either no association or a weak association between the variables among studies measuring this associations. Accordingly, the evidence is insufficient to prove the association between GMS and IC in healthy preschoolers. It is necessary to conduct additional studies. Preschoolers are at an important stage of developing GMS and IC (Garon et al., 2008; Tomaz et al., 2019). A favorable relationship between GMS and IC in healthy preschoolers can serve as a basis for future studies to understand the mechanisms for this relationship and to serve as a rationale for initiating intervention studies designed to improve GMS in preschool children.

The purpose of this study was to examine the relationships between GMS (total, LS, and OCS) and IC (IC-accuracy, IC-reaction time) scores obtained from the Fish Flanker task in healthy preschool children, ages 4–6 years. Based on a previous studies of GMS and IC in 5- and 6-year-old young children (Livesey et al., 2006), we hypothesize that GMS and IC scores obtained from standardized tests are negatively related.

MATERIALS AND METHODS

Participants and Inclusion Criteria

The present study analyses cross-sectional, baseline data from The Influence and Mechanism of Aerobic Exercise on Preschool Children's Executive Functions: A Randomized Controlled and Iconography Studies (Trial Registration: Chi CTR1900021552). The purpose of the above referenced study was to investigate the effects of an aerobic exercise intervention on the executive functions of preschool children. A total of 126 children aged 4–6 years (boys, 68; girls, 58) were recruited from preschools from four urban kindergartens in the Yangpu District of Shanghai, China. The preschools organized meetings with the students' parents and/or guardians to explain the purpose and details of the study and to receive their assent for students to participate in the study. Inclusion criteria were as follows: (1) preschoolers aged 4–6 years; (2) good health with no contraindications to exercise, such as cardiovascular, neurological, or endocrine disease; and (3) receipt of informed assent forms signed and submitted by parents and/or guardians. The Ethics Committee of Shanghai University of Sport has approved this study (code: 2017023).

Procedure and Measurements

Data Collection and Research Setting

All study activities were conducted from 9:00 to 11:00 am in participants' kindergarten classes. The GMS and IC trials were implemented in a fixed sequence by a trained assessor and a trained assistant. To minimize the sources of measurement error, all tests were conducted by the same assessor. Parents and/or guardians completed demographic questionnaires developed for this study to collect information about the parent's and/or guardian's gender, age in years (y), maternal education (high school, college/associate degree, bachelor's degree, master's degree, doctoral degree), Annual per capita household income (< 9,000 RMB/per capita; 9,000 to 30,000 RMB/per capita; 30,001 to 100,000 RMB/per capita; and > 100,000 RMB/per capita) (1 RMB ≈ 0.16 US dollars), and the number of preschooler's extracurricular classes taken outside of school (e.g., basketball, dancing, and badminton classes). Height in centimeters (cm) and weight in kilograms (kg) were measured on laboratory scales using procedures for preschool children identified in the National Physical Fitness Measurement Standards Manual (The General Administration of Sport of China, 2003). Body Mass Index (BMI, kg/m^2) was computed as weight kg/height cm^2 and the classification of BMI according to International Obesity Task Force (Cole et al., 2000).

Fish Flanker Task

A computerized Fish Flanker task was utilized to measure preschoolers' IC and was implemented on E-Prime software (version 2.0, Psychological Software Tools, Pittsburgh, PA, United States). The Flanker paradigm has been described previously (Mcdermott et al., 2007). Briefly, the Fish Flanker task presents stimuli in a horizontal row of five fish with different orientations classified as a consistent condition (i.e., the direction of the fish is the same for all the fish) or as an inconsistent condition (i.e., more than one direction of the fish is observed). The goal of the task is to correctly identify if the direction of the middle fish (target fish). Standardized and age-appropriate instructions were used to convey the rules of the task to the participants. For example, children were asked "These fish are having fun. Please look at the fish in the middle that is hungry. If the middle fish is facing to the left, press the left button to feed it. If the middle fish is facing to the right, press the right button to feed it." **Figure 1** shows an image of the Fish Flanker task.

The Fish Flanker IC scores are presented as the time in milliseconds (ms) it takes to respond to the correct stimulus (IC-RT), presented as the average time across trials, and percent accuracy of responses (IC-ACC), computed as a percent (total number of trials divided by the number of correct trials). All participants completed the task as directed by experienced assessors in a quiet classroom setting. Participants were asked to respond as quickly as possible to the target fish on the screen independent of the fish to either side of the target fish (flanking fish) by pressing a button according to the direction of the target fish. A marker flashed for 500 ms at the beginning of the task as a cue that a target fish selection task would follow. The fish stimuli would be substitute by next fish stimuli after a response was made or until a response time more than 3000 ms. Tests were separated by 1500 ms. Prior to starting the trial, participants completed 20 practice tests with a goal to achieve 80% of the fish selected accurately. A total of 120 experimental trials were completed after the practice trials. An equal numbers of consistent and inconsistent trials were randomly intermixed and balanced such that all types of stimulus-flanker pairings were equally likely to occur. Participants were given a break of 5 min after their practice and after every 40 experimental trials. The participant's performance for IC-ACC and IC-RT on the Fish Flanker tasks was recorded on the computerized E-Prime software (Martins et al., 2020). Data were considered invalid and were not included in the statistical analyses when participants pressed any key on the keyboard other than the directional < or > keys and when the reaction time was less than 200 ms or more than 3 s.

Test of Gross Motor Development Skills

Gross motor skills were measured by using the Test for Gross Motor Development (2nd edition, TGMD-2) which is globally viewed as the gold standard for GMS assessment with excellent test-retest reliability (Griffiths et al., 2018). The validity and reliability of TGMD-2 has been established for Chinese children (Li and Ma, 2007). The rater's reliability, internal-consistency reliability and test-retest reliability of the TGMD-2 are r = 0.62 to 0.86, r = 0.72 to 0.89 and r = 0.87 to 0.94, respectively. Compared the final physical education scores, there are significant relationship between the final physical education scores and TGMD-2 score. TGMD-2 is comprised of two subtests (LS and OCS) with each subtest composed of six skills. The LS portion assesses running, galloping, hopping, leaping, jumping horizontally, and sliding. The OCS portion assesses striking a stationary ball, dribbling (bouncing) a stationary ball, kicking and catching a ball, throwing a ball overhand, and rolling a ball underhand. Prior to testing, assessors were trained on how to administer and evaluate each test performed according to the TGMD-2 training manual (see **Supplementary Material**). Also, videos were made to assist assessors in evaluating the skills. The inter-rater reliability of the assessors was high (ICC = 0.85, 95% CI = 0.73–0.92). Participants were tested in groups with six children per group. Participants waiting to perform their trials remained in the classroom and completed their regular lessons. Prior to the participants performing the tests, researchers demonstrated the correct form and procedures for each of the 12 skills. Participants performed each GMS skills' test twice. Participants were scored according to the presence (score of 1) or absence (score of 0) of each criterion demonstrated during the test trials. Scores from each skill were added to obtain a total subtest score for the LS and the OCS portions of the total GMS score. The highest possible score for each LS and OCS subtest was 48. The two subtest scores were added to create the total GMS score with maximum score of 96.

Statistical Analysis

Participant and parent and/or guardian characteristics are described as the mean and standard deviation (± SD) for continuous variables and the frequency (number and percentage) for categorical variables. Independent sample t-test were used to evaluate gender

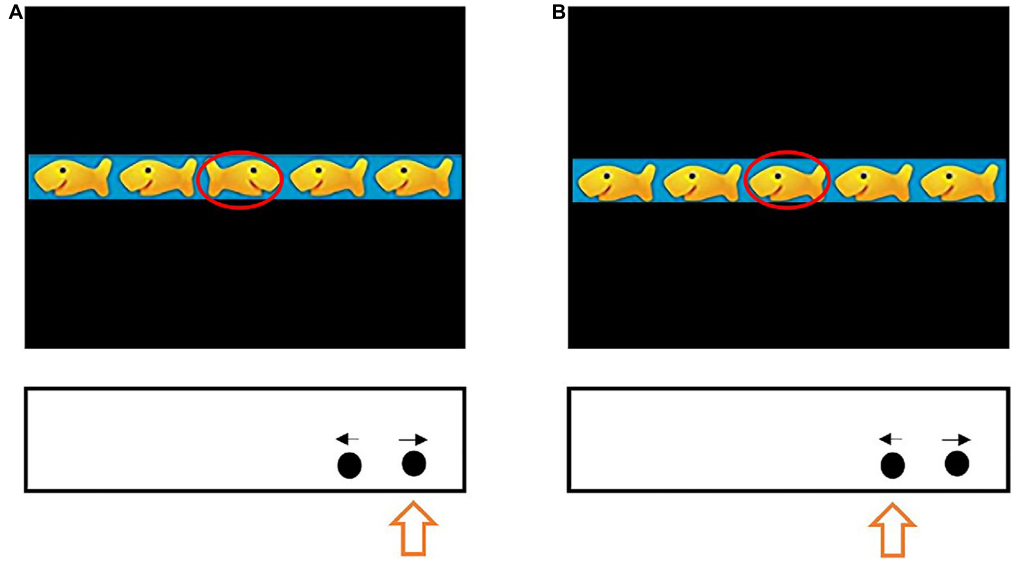

FIGURE 1 | Fish flaker task.

differences between the continuous and categorical variables, respectively.

A multivariate linear regression model was used to test the hypothesis that total GMS and subtests of LS, and OCS are significantly related to IC-ACC and IC-RT scores. Total GMS, and its' subtests (LS, OCS) entered as independent variables, and IC (IC-ACC, IC-RT) entered as dependent variable in analysis. Two steps of analyses were performed. GMS scores entered as continuous variables in the first step and the GMS scores were categorized into Tertiles in the second step. In each analysis, data were computed as unadjusted (model 1) and adjusted analyses (model 2). In adjusted analyses, data were adjusted for potential confounders of age, BMI, gender, maternal education, household income, and the number of children's extracurricular classes. In the first step of analysis, multivariate linear regression models with continuous independent and dependent variables are interpreted as follows: for each 1-point increment in the independent variable (total GMS, LS, OCS), there is an accompanying increase or decrease in the dependent variable (IC-ACC, IC-RT) with the amount of change determined by the direction and size of the beta coefficient.

In the second step of analysis, total GMS, LS, and OCS were divided into Tertiles with T1 containing the lowest scores and T3 containing the highest scores. The interpretation as follows: compared with the lowest scores T1, the dependent variable (IC-ACC, IC-RT) of T2 and/or T3 group improved or reduced. Unadjusted and adjusted multiple linear regression models tested the relationships between Tertiles of total GMS, LS, and OCS (T1 = referent group) with the continuous IC-ACC and IC-RT scores. Statistical analyses were performed with SPSS Statistics 22.0 (IBM, Armonk, NY, United States) and EmpowerStats software (www.empowerstats.com, X&Y solutions, Inc., Boston, MA, United States). $P < 0.05$ was accepted as statistically significant.

RESULTS

Among the 126 participants who completed the Fish Flanker task and TGMD-2 tests, data from 123 participants (68 boys and 55 girls; mean age, 4.89 ± 0.39 years) are included in the analysis (**Figure 2**). Three girls were excluded from data analysis due to their parents' disapproval of testing subsequent to providing assent for their preschoolers to participate in the study. Characteristics of participants and parents and/or guardians, the GMS, and the IC scores are presented in **Table 1**. The majority of participants (83.06%) had a normal BMI according to the International Obesity Task Force (Cole et al., 2000). Height, weight, and BMI were higher in boys than girls ($P < 0.01$ to 0.05). LS scores for sliding were higher in girls than boys ($P < 0.05$) and OCS scores for striking and kicking skills were higher in boys than girls ($P < 0.05$). No significant differences by gender were observed for the remaining variables ($P > 0.05$).

In the first step of analyses with total GMS, OCS, and LS scores analyzed as continuous variables, beta coefficients for total GMS, LS, and OCS scores were significantly and inversely related to IC-RT in model 1 ($P < 0.05$) and in model 2 ($P < 0.05$) (**Table 2**). None of the beta coefficients for the total GMS, LS, and OCS were related to IC-ACC ($P > 0.05$). For interpretations, after controlling for potential confounders in model 2, each 1-point increment in the total GMS, LS, and OCS scores resulted in a reduction in IC-RT by 8.27 ms (95% CI: −14.2, −2.34), 11.2 ms (95% CI: −21.43, −0.97), and 12.15 ms (95% CI: −22.07, −2.23), respectively.

In the second step of analysis with the total GMS, LC, and OCS scores divided into Tertiles, beta coefficients for T3 total GMS (models 1 and 2) and T3 LS (model 1) were negatively related to IC-RT ($P < 0.05$). Beta coefficients for T2 total GMS (model 2) and T3 LS (model 1) were positively related to IC-ACC ($P < 0.05$). For interpretations, T2 total GMS scores (model 1)

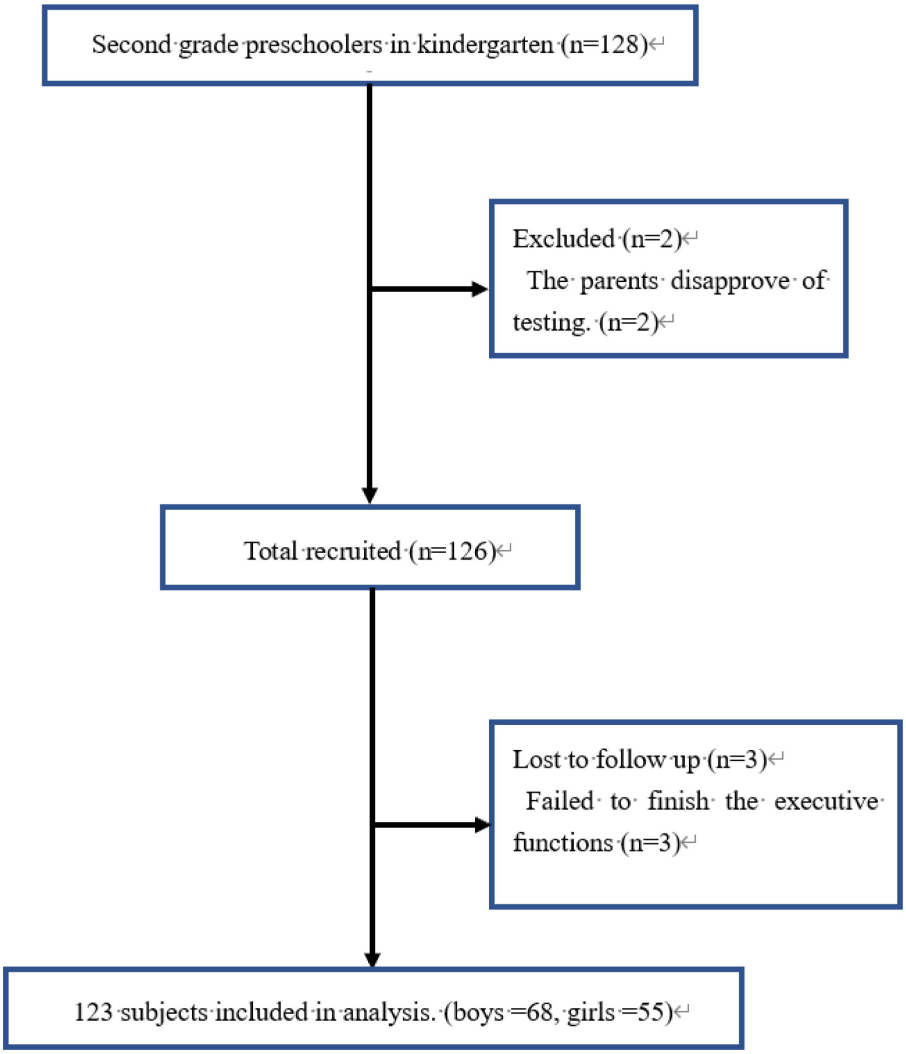

FIGURE 2 | Flowchart of the subjects in the present study.

were associated with a 6.18% (95% CI, 0.62, 12.29) higher IC-ACC score ($P < 0.05$), compared to T1 total GMS scores. T3 total GMS scores (model 2) resulted in a reduction in IC-RT by −216.98 ms (95% CI: −357.39, −76.57; $P_{\text{trend}} < 0.01$), compared to T1 total GMS scores.

DISCUSSION

This study aimed to investigate the relationships between GMS (total GMS, LS, and OCS) and IC (IC-ACC and IC-RT) in healthy preschool-age children ages 4-6 years. When analyzed as a continuous variable, total GMS, LS, and OCS scores showed significant and negative associations with IC-RT, indicating the preschool-age children with higher GMS scores spent less time selecting the correct answer on the Fish Flanker IC task than preschool age children with lower GMS scores ($P < 0.05$). Total GMS scores divided into Tertiles showed a positive association between the T2 total GMS and IC-ACC scores and a negative association for T3 total GMS scores and IC-RT, indicating total GMS scores were related to speed and accuracy on the Fish Flanker task in preschool-age children ($P < 0.05$).

Few studies have evaluated the associations between motor skills and EF in children and adolescents. Mora-Gonzalez et al. (2019) showed that muscular fitness, speed agility, and cardiorespiratory fitness were related to EF in overweight and obese children aged 10.1 ± 1.1 years. Salcedo-Marin suggested that EF planning functions are mediated by various processes, such as cognitive processing speed and motor coordination in children and adolescents, ages 8-17 years, with attention deficit hyperactivity disorder (Salcedo-Marin et al., 2013). Ludyga et al. (2019) showed that OCS scores were inversely related to IC-RT in healthy, preadolescent children, ages 10-12 years. The present study showed similar associations in preschool children, ages 4-6 years, with total GMS, LS, and OCS scores negatively associated with IC-RT and Tertiles of total GMS T2 related to IC-ACC.

TABLE 1 | Characteristics of participants and parents and/or guardians and Gross Motor Skills and Inhibitory Control scores.

Variable	Girl (*n* = 55)	Boy (*n* = 68)	Total (*n* = 123)	*P* for sex
Basic Demographic information				
Age (years)	4.93 ± 0.42	4.86 ± 0.36	4.89 ± 0.39	0.32
Male sex, n (%)			68 (55.28%)	
Anthropometric characteristics				
Weight (kg)	18.58 ± 2.42	20.42 ± 3.39	19.60 ± 3.12	**< 0.01**
Height (cm)	109.83 ± 4.74	111.79 ± 4.90	110.91 ± 4.91	**0.03**
BMI (kg/m^2)	15.36 ± 1.31	16.29 ± 2.11	15.88 ± 1.85	**< 0.01**
Normal	52 (94.55%)	53 (77.94%)	105 (85.37%)	
Overweight	3 (5.45%)	9 (13.24%)	12 (9.76%)	
Obesity	0 (0.00%)	6 (8.82%)	6 (4.88%)	
Socioeconomic status				
Household income (annual per capita RMB) n, (%)				0.65
< 9,000	5 (10.20%)	4 (6.06%)	9 (7.83%)	
9,000-30,000	7 (14.29%)	13 (19.70%)	20 (17.39%)	
30,001-100,000	18 (36.73%)	20 (30.30%)	38 (33.04%)	
>100,000	19 (38.78%)	29 (43.94%)	48 (41.74%)	
Maternal education, n (%)				0.69
High school	1 (2.04%)	2 (3.03%)	3 (2.61%)	
College/Associate's degree	3 (6.12%)	8 (12.12%)	11 (9.57%)	
Bachelor's degree	13 (26.53%)	12 (18.18%)	25 (21.74%)	
Master's degree	26 (53.06%)	34 (51.52%)	60 (52.17%)	
Doctoral degree	6 (12.24%)	10 (15.38%)	16 (13.91%)	
Extracurricular class, n (%)				0.94
Yes, n (%)	33 (67.35%)	44 (66.67%)	77 (66.96%)	
No, n (%)	16 (32.65%)	22 (33.33%)	38 (33.04%)	
Inhibitory control				
Accuracy (ICC-ACC) (%)[a]	86.51 ± 14.76	86.06 ± 13.58	86.01 ± 14.05	0.38
Reaction time (ICC-RT) (ms)[b]	1236.34 ± 296.89	1233.16 ± 306.27	1240.31 ± 301.64	0.88
Total GMS (Score)	71.93 ± 10.09	71.85 ± 10.10	71.78 ± 9.95	0.84
Locomotor (Score)	38.18 ± 4.93	36.55 ± 6.59	37.28 ± 5.88	0.34
Run	6.95 ± 1.13	7.22 ± 0.99	7.10 ± 1.06	0.20
Gallop	6.85 ± 2.01	6.43 ± 2.56	6.62 ± 2.33	0.55
Hop	5.44 ± 2.17	4.81 ± 2.67	5.09 ± 2.47	0.23
Leap	5.38 ± 1.05	5.41 ± 1.05	5.40 ± 1.05	0.90
Horizontal Jump	6.40 ± 1.71	6.38 ± 1.79	6.39 ± 1.74	0.95
Slide	7.07 ± 1.44	6.37 ± 2.20	6.68 ± 1.92	**0.04**
Object-control (Score)	33.75 ± 7.09	35.30 ± 5.67	34.50 ± 6.26	0.17
Strike	7.38 ± 2.09	8.09 ± 1.71	7.77 ± 1.91	**0.04**
Stationary Dribble	5.49 ± 2.28	5.37 ± 2.29	5.42 ± 2.28	0.15
Catch	3.65 ± 1.60	3.65 ± 1.60	3.72 ± 1.51	0.92
Kick	5.93 ± 1.26	6.49 ± 1.25	6.24 ± 1.28	**0.02**
Overhand Throw	5.58 ± 2.07	6.19 ± 1.67	5.92 ± 1.88	0.07
Underhand Roll	5.33 ± 2.09	5.51 ± 1.88	5.43 ± 1.97	0.70

[a]IC-ACC is computed by dividing the total number of tests performed by the number of tests with correct selections. [b]IC-RT is the average reaction time of correct selections.
GMS, gross movement skill; BMI, Body Mass Index. The mean ± SD was reported for normal or non-normal distribution variables. The bold font is used to highlight significance level at $P < 0.05$.

While the results obtained from this study preclude identifying a causal association between GMS and IC, they are consistent with other studies observed in children and youth of different ages, health status, and developmental conditions.

Examination of studies investigating the associations between GMS and IC in preschoolers highlight the difficulty of comparing results obtained with varied methods and measurement scales. For example, in the present study, GMS was measured with the TGMD-2 and IC for task speed and accuracy was measured with the Fish Flanker task. Cook et al. (2019) measured GMS with the TGMD-2 and IC with the Go/No-Go tests. They reported positive and significant associations between LS ($\beta = 0.2$,

TABLE 2 | Associations between gross motor skill (Total GMS, LC, and OCS) presented as continuous scores and in Tertiles with inhibitory control scores (IC-ACC and IC-RT) on the Fish Flanker Test in preschool children ages 4-6 years (*N* = 123).

Variable	IC-ACC (accuracy),β (95%CI)		IC-RT (reaction time),β (95%CI)	
	Model 1	Model 2	Model 1	Model 2
Total GMS (Score)	0.24 (−0.01, 0.48)	0.09 (−0.16, 0.33)	**−6.08 (−11.35,−0.80)**	**−8.27 (−14.20,−2.34)**
Total GMS tertile (Score)				
T1 (42-70)	0 (Ref)	0 (Ref)	0 (Ref)	0 (Ref)
T2 (71-76)	**7.71 (1.73, 13.69)**	**6.47 (0.62, 12.33)**	−70.56 (−198.94, 57.81)	−109.35 (−250.13, 31.43)
T3 (77-92)	4.06 (−1.92, 10.04)	2.40 (−3.44, 8.23)	**−154.66 (−283.04,−26.29)**	**−216.98 (−357.39,−76.57)**
P for trend	0.092	0.25	**0.02**	**<0.01**
Locomotor (Score)	0.40 (−0.02, 0.83)	0.10 (−0.32, 0.53)	**−10.62 (−19.55,−1.70)**	**−11.20 (−21.43,−0.97)**
Locomotor tertile (Score)				
T1 (19-35)	0 (Ref)	0 (Ref)	0 (Ref)	0 (Ref)
T2 (36-40)	2.83 (−3.22, 8.87)	−1.37 (−7.46, 4.71)	−35.83 (−165.68, 94.01)	−18.85 (−166.68, 128.97)
T3 (41-46)	**6.18 (0.06, 12.29)**	1.27 (−4.80, 7.33)	−114.03 (−245.38, 17.31)	−116.97 (−264.37, 30.42)
P for trend	**0.05**	0.68	0.09	0.12
Object-control (Score)	0.24 (−0.16, 0.64)	0.14 (−0.28, 0.55)	−6.01 (−14.51, 2.49)	**−12.15 (−22.07,−2.23)**
Object-control tertile (Score)				
T1 (13-32)	0 (Ref)	0 (Ref)	0 (Ref)	0 (Ref)
T2 (33-37)	4.41 (−1.84, 10.66)	1.73 (−4.49, 7.96)	−58.86 (−193.34, 75.62)	−60.76 (−211.30, 89.78)
T3 (38-46)	0.74 (−5.41, 6.90)	−0.56 (−6.93, 5.81)	−62.67 (−195.07, 69.72	−147.55 (−301.63, 6.52)
P for trend	0.73	0.96	0.34	0.07

Ref, Referent; GMS, gross movement skill; CI, confidence interval; The β values are standardized; The bold font is used to highlight significance level at P < 0.05; Model 1: Unadjusted; Model 2: Adjust for sex, age, BMI, maternal education, number of participants' extracurricular classes, and per capita household income.

P = 0.047) and OCS (β = 0.24, *P* = 0.024) scores and IC- ACC in preschoolers. Livesey et al. (2006) measured GMS with the Movement Assessment Battery for Children test and IC using the Modified stop-signal task. They observed a modest association between OCS and IC-ACC in preschoolers ($r = 0.454$, $P < 0.05$). In contrast, null relationships between GMS and IC-ACC were identified in the present study ($P > 0.05$). There are several reasons which may account for these inconsistent results. First, the psychological tasks used to assess IC differed in the types of IC assessed (Response Inhibition and Attention Inhibition) which are related to different neural networks in the brain (Verbruggen and Logan, 2008). The Go/No-go (Cook et al., 2019) and Stop-signal tasks (Livesey et al., 2006) are used to measure Response Inhibition which is related to the lateral and orbital prefrontal cortex. The Flanker task used in the present study and the Stroop test assess Attention Inhibition which is associated with anterior cingulate, dorsolateral prefrontal cortex and basal ganglia (Nigg, 2000). Second, the types of tests used to measure GMS skills differ between product- (e.g., jump height) and process-oriented (e.g., technique) outcomes. Livesey et al. (2006) used the Movement Assessment Battery for Children which is product-oriented whereas Cook (Cook et al., 2019) and the present study used the process-oriented TGMD-2 GMS test. Beside the results affected by the types of GMS and IC measures, socioeconomic status is an important factor between the development of GMS and IC processes in preschool-age children (Santos et al., 2008). The participants in the Cook et al. (2019) study were from a low- socioeconomic status population in South African settings, whereas the participants in the present study were from medium-to-high income Chinese families with a majority of their mothers (97.39%) having a college education. To establish consistency of results in future studies, researchers should strive to use the same measurement scales to assess GMS and IC.

Possible Mechanism

Biological mechanisms for the associations between GMS and IC are based on evidence showing that areas of the brain involved in IC are closely related to motor pathways (Rae et al., 2015). Ludyga et al. (2021) reported an overlap in the neural networks between GMS and IC regions of the brain. The IC pathway involves the anterior cingulate, dorsolateral prefrontal cortex, and basal ganglia areas in the brain. Basal ganglia are highly involved in GMS as they contribute to inhibition of unnecessary movement and are important in mobilizing and coordinating body movements (Thach et al., 2000; Piek et al., 2004). In an animal study, Adkins et al. (2006) observed that motor training led to synaptogenesis synaptic potentiation, and reorganization of movement representations within the motor cortex. This is relevant as synapses affect the transmission efficiency of information (Cartling, 2002) and are related with cognitive development (Choi et al., 2018). Evidence shows that GMS shares common underlying processes with IC observed in sorting, monitoring, and planning tasks (Boxtel et al., 2001). Therefore, the skills which are acquired by preschoolers during the process of improving and mastering GMS may involve a transfer to the response processes of the brain related to IC. Booth et al. (2013) have reported that development of GMS facilitates physiological changes in the brain and improves the reaction ability of IC in preschoolers. Thus, IC-RT as a general measure of information processing speed may share a common underlying neurocognitive mechanism with GMS. The present results showing negative associations between GMS measures and IC-RT are consistent with the observation by Booth et al. (2013). Additional studies are needed to better understand the neurophysiology and mechanisms mediating the associations between GMS and IC.

Applications

As it is necessary for preschoolers to pay attention to information, such as their location in space and the environment around them, it is important they learn how to restrain from attending to unrelated-goal behaviors in various settings, including during exercise. Having a fast cognitive reaction time means preschoolers spend a shortest time making a correct answer which reflects attention and is closely associated with executive functions (De Greeff et al., 2018). As evidence supports associations between GMS and IC, performing motor coordination tasks, and exercises that develop locomotor and object control skills should be encouraged in preschoolers. Activities that enhance motor coordination and GMS contribute to EF and IC by enhancing the efficiency of neurocognitive processing and the allocation of attentional resources in children's immature brain states (Chang et al., 2013).

Strengths and Limitations

To the best of our knowledge, few published studies (Van der Fels et al., 2015) of the relationship between GMS and IC have focused on healthy preschool children and those that have used GMS and IC tasks that differ from those used in the present study. Existing studies measure the accuracy of IC tasks, but none have measured the speed of completing an IC task. A strength of the present study is that it used valid and reliable GMS and IC tests to determine the association between total GMS, LS, and OCS abilities with EF IC-ACC and IC-RT in preschoolers with a wide range of motor skills.

There were also limitations associated with the present study, including a relatively small sample size of 123 preschool-aged children and the cross-sectional design. The cross-sectional design prevented causal relations from being drawn between GMS and IC. Furthermore, the participants in this study were Chinese and mostly from medium- or high-income communities, and a majority of their mothers received higher education. This corresponded with the participants receiving high IC-ACC scores (mean $\pm$ SD: 86.01 $\pm$ 14.05), indicative that the trial was very easy for them. Additional studies with similar participants are needed to confirm these results.

CONCLUSION

In summary, the results of this study demonstrated a negative relationship between total GMS components of locomotor and object control skills with the executive functions IC subsets of reaction time, and to a lesser extent, accuracy in responding to the Fish Flanker task in preschool children. The results provide further support for the hypothesis that GMS are related to specific aspects of IC and they highlight the importance of teaching motor skills to preschoolers. As the biological mechanisms between GMS and IC are not fully understood, research showing the variables may share common underlying biological processes is promising and calls for further studies designed to understand how motor skills are related to cognitive process of EF, and in particular, IC-RT. Cross-sectional, prospective, and experimental studies in preschoolers are encouraged to use the same measurement scales to confirm the results GMS and IC obtained in this study.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Ethics Committee of Shanghai University of Sport (code: 2017023). Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

AUTHOR CONTRIBUTIONS

JJL: conceptualization, validation, formal analysis, and writing—original draft preparation. MQ: methodology and resources. WH, CF, and LL: software. YYL, MS, YHL, WH, CF, LL, XS, and TZ: investigation. JJL and MQ: data curation. XS and MQ: writing—review and editing. JYL: visualization, supervision, project administration, and funding acquisition. All authors have read and agreed to the published version of the manuscript.

FUNDING

This research was funded by Shanghai Educational Science Research Project (C19052), the National Natural Science Foundation of China (81703252), and the National Key Research and Development Program of China (2020YFC2003301).

ACKNOWLEDGMENTS

We thank all the participants and kindergarten very much for their collaboration.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fnhum.2022.848230/full#supplementary-material

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frontiers | Frontiers in Human Neuroscience

TYPE Original Research
PUBLISHED 12 August 2022
DOI 10.3389/fnhum.2022.926346

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OPEN ACCESS

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SPECIALTY SECTION
This article was submitted to Cognitive Neuroscience, a section of the journal Frontiers in Human Neuroscience

RECEIVED 22 April 2022
ACCEPTED 18 July 2022
PUBLISHED 12 August 2022

CITATION
Wang S, Chen D, Yoon I, Klich S and Chen A (2022) Bibliometric analysis of research trends of physical activity intervention for autism spectrum disorders.
Front. Hum. Neurosci. 16:926346.
doi: 10.3389/fnhum.2022.926346

Bibliometric analysis of research trends of physical activity intervention for autism spectrum disorders

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Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by social impairment, restricted interests, and repetitive stereotyped behaviors. At present, its pathogenesis has not been fully understood. Various methods are used for clinical treatment and intervention, among which physical activity (PA) intervention also has an obvious effect. This study has used bibliometric methods and visual analysis methods to analyze 885 studies of PA intervention in ASD from 2003 to 2022 in the Web of Science (WoS) database in order to provide theoretical support for the follow-up research on the effect of PA with ASD. The main findings of this study are as follows. First, the literature on PA interventions in ASD research showed a growing trend. The leading institution in this field is the University of Delaware, forming a core group of authors represented by authors such as Sean Healy and Carol Curtin et al. Second, the research focus of this research area mainly includes PA interventions for children and adolescents with ASD. PA can improve symptoms such as stereotyped behaviors and motor function in patients with ASD as well as can reduce childhood obesity rates and improve quality of life. Third, skill, youth, prevalence, and meta-analysis systematic reviews were found. It is the long-term concern and focus of researchers. In conclusion, the current research is only a short-term analysis, and it is not possible to verify the long-term effect; thus, future data analysis should evaluate and explore the long-term effects of PA interventions on ASD including cohort and longitudinal study types focused on the rehabilitation of patients with ASD. Moreover, testing the sustainability of benefits for children with ASD and constructing a multidimensional exercise integrated intervention model are the main directions for future research in this field.

KEYWORDS

bibliometric analysis, research trend, physical activity, autism spectrum disorders, CiteSpace, hotspots and frontiers

Introduction

Autism spectrum disorder (ASD) is a lifelong neurodevelopmental disorder that limits or impairs daily functioning characterized by social communication, social interaction disorders, narrow interests, and repetitive stereotypes (Association American Psychiatric, 2013). The prevalence of ASD is increasing every year, while it usually has a high lifetime disability rate (Hodges et al., 2020). According to the Centers for Disease Control and Prevention, the prevalence of ASD has increased from 2 per 10,000 children to 1 per 54 children over the past 20 years (Maenner et al., 2020). For more than half a century, multidisciplinary research has been devoted to exploring the causes and pathogenesis of ASD, but, so far, it has not been explained, so there is no definitive curative treatment.

Studies in neuroscience have linked physical activity (PA) to brain structure and cognitive development in recent years (Donnelly et al., 2016). Previous systematic reviews and meta-analyses have shown a positive effect of PA interventions on cognitive function, especially on working memory, selective attention inhibition, and cognitive flexibility (Álvarez-Bueno et al., 2017). The positive effect on cognitive function is related to an increase of brain-derived neurotrophic factors, thereby promoting learning and maintaining cognitive function by improving synaptic plasticity and electrical stimulation of a nerve and increasing cerebral circulation (Hillman et al., 2008). Moreover, the PA has an important effect on cognitive function in patients with ASD. Pan et al. (2017) significantly reported higher motor skill proficiency and executive function after 12 weeks of PA intervention in children with ASD. Moreover, a large number of experimental studies have also found that PA interventions can improve social interaction disorders, stereotyped behaviors (Teh et al., 2021), language disorders (Zeng et al., 2017), athletic ability (Cai et al., 2020; Park et al., 2021), behavioral management (Greco and De Ronzi, 2020), and lowering body fat (Sefen et al., 2020). PA is increasingly valued as an intervention method without adverse reactions. It promotes an increase in the review studies of PA intervention in ASD.

As a medium for documenting research results, a review is an important source of theoretical results. Through the review, the research trends and their development status can be clearly understood, laying the foundation for future scientific research. So far, scholars have published a number of different studies that investigated the effect of PA intervention in ASD, and how to extract information from many existing studies and clarifying the research status and development trend in this field is a valuable Research Topic. The bibliometric analysis uses quantitative methods to examine the structure and development of different disciplines and is a process of evaluating and predicting the current situation and development trends in the research field using measurement methods such as mathematics and statistics (Zupic and Cater, 2015; Van Raan, 2019). Through the analysis of institutions, authors, and keywords in bibliometric analysis (Yu et al., 2017), scholars are able to obtain the research status and trends of PA intervention in ASD research. Quantitative analysis of the literature to determine differences between studies in different regions and the merits of author collaboration (Ellegaard and Wallin, 2015) both circumvents the bias of researchers and has the advantage of identifying important research content (Pesta et al., 2018).

In recent years, many researchers have conducted a large number of bibliometric analysis studies on ASD by using bibliometric analysis. Reviewing the findings related to this study objective, Sweileh et al. (2016) conducted an author collaboration network analysis of global ASD studies using bibliometric methods, revealing the characteristics and trends of domain collaboration. Wang et al. (2020) found that *de novo* mutations (DNMs) are a hot topic in the field of ASD research in recent years and believe that genetic information is an important research trend in the field of ASD research. Shekarro et al. (2021) analyzed the institutional and author partnerships, citations, and funding funds of ASD executive function research, providing a reference for subsequent authors to understand the knowledge structure and development trend of ASD executive function research.

In summary, bibliometrics has been successfully applied in the research field of ASD, but most of the existing studies are more comprehensive bibliometric analyses in the field of ASD research, and the specific research results of PA intervention in ASD research have not yet appeared. Therefore, it is necessary to summarize the latest progress and research direction and hotspot of PA intervention in ASD. In this case, a thorough understanding of PA intervention in the ASD research process is very important.

Therefore, the main aim of this study was to investigate both bibliometric and visual analysis methods to systematically analyze all the processes and reviews of PA interventions in ASD research included in the Web of Science (WoS) database. Understanding the structure, status, and future direction of the current PA intervention in ASD research will stimulate scholars to discover new problems and lay a further foundation for exploring intervention methods.

Methods

Data selected

The data in this study were derived from the core collection of WoS, an interdisciplinary comprehensive academic information database of the American Institute for Scientific Information (ISI), which were collected and screened through the WoS database. Based on the relevant prior studies (Healy et al., 2018), the search formula for this study was TS =

(Autism spectrum disorder) AND TS = [physical activity (PA) intervention OR exercise rehabilitation OR exercise therapy OR exercise intervention OR physical activity OR exercise], file type was article or review, and the retrieval period was Searchable document start-2022.03.01 By reading the abstract and content of the article, the output literature data were manually screened and processed. Finally, 885 valid documents were obtained, and the search results of these documents were exported to the format required for CiteSpace operation, whose research data were used in this study.

Data analysis methods

Bibliometric analysis methods

Bibliometric methods were quantitative and qualitative combinations of the number of authors, word frequency statistics, and citations in the literature (Zupic and Cater, 2015; Van Raan, 2019). In this study, publication time, institutions, authors, and keywords of studies were used to objectively evaluate the research status of PA intervention in ASD using the bibliometric analysis method.

Data visualization methods

Data visualization methods were used to demonstrate graphical means to clearly and effectively convey and communicate information (Azzam et al., 2013). In this study, the CiteSpace (5.6.R1) (Chen, 2014) visual analysis software was used to visualize the development trend of PA intervention in ASD research. The CiteSpace is a visual analysis program developed by Professor Chaomei Chen of Drexel University based on JAVA, which has been widely used in visual analysis research in various fields of knowledge since its development. This study used CiteSpace to map the collected data in co-institutions' network analysis, co-author analysis, and keyword analysis. Thus, the research process and current situation of PA intervention in ASD research were explored, and the trend of future development was predicted. Based on the above, this research technology roadmap is shown in Figure 1.

Result

Basic statistical analysis

Published trend analysis

The amount of writing may show the degree of attention of a certain subject area, and the continuous number of articles issued year by year may reflect the change in the degree of attention in the subject area. The number of literature published about ASD research from 1 January 2003, to 1 March 2022, showed a total of 885 articles. The number of articles published also showed a trend of increasing year by year (Figure 2), which was roughly divided into 3 stages. The first phase was the initial phase (2003–2013) from 1 article (2003) to 19 articles (2013), and a total of 81 articles were published during the 10 years, accounting for a total of 9.16%. The second phase was the slow growth phase (2014–2018), which increased from 44 articles (2014) to 130 articles (2018) during the 4 years, and a total of 284 articles were published, accounting for a total of 32.09%. The third phase was the high-speed phase (2019–2021), which increased from 130 articles (2019) to 204 articles (2021) during the 3 years, and a total of 496 articles were published, accounting for a total of 56.05%. During the period from 2003 to 2021, the literature on PA interventions in ASD research grew 200-fold. According to the publication trend, it is foreseeable that in the future, the number of relevant articles on PA intervention in ASD remains around 200–300 per annum. Note that the number of articles published in 2022 was 24 (2.7%) for the first 3 months of posting statistics.

The trend in publication volume shows that many researchers are gradually paying attention to the impact of PA on ASD. The reason for the increase in retrospective literature is largely related to the development and implementation of research measurement tools and research projects. In this study, although the rapid update of research measurement tools has made it difficult to track their specific time, the reason for the rapid increase in the number of studies since 2014 is closely related to brain programs implemented in countries around the world, such as the Human Brain Project (HBP), BRAIN Initiative, Brain/Minds Project, Brain Science and Brain-Like Intelligence Technology (China Brain Project), and other research projects oriented to tackling brain diseases. It has contributed to a significant increase in the amount, form, and latitude of data generated by new neuroscience instruments using imaging and activity recording, as well as an increased reliance on new technologies and analytical methods that utilize neuroscience data. For example, consider the HBP that aims to summarize the knowledge currently available to the human brain and gradually build models through supercomputers to simulate the human brain. The integration of neuroscience, medicine, and computer technology will enable humans to finally understand brain and brain diseases and offer new perspectives for future computers and robotics (https://www.humanbrainproject.eu/en/). These brain programs have not only promoted the innovation of imaging technology but also enabled humans to overcome unresolved brain diseases, indirectly increasing the number of publications in the field of PA intervention in ASD research.

Co-institutions' network

The use of CiteSpace generated a network as usual: 2003–2022; Slice length: 1 year; Select the node type: Institution; Top N = 50; and Choice: Pathfinder and Pruning the merged network. Other parameters were the default settings. In addition,

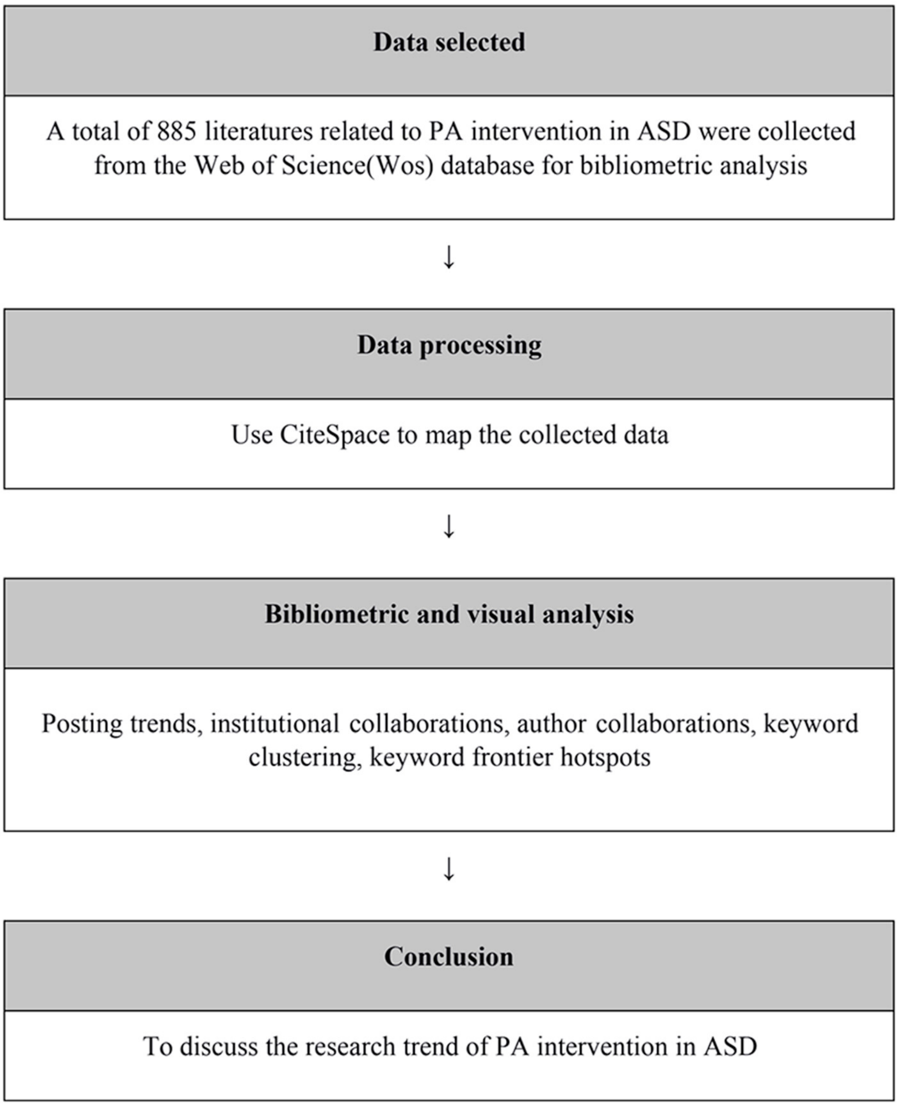

FIGURE 1
Process flow.

the co-institutions' knowledge mapping was generated, in which N = 143 and E = 140 (density was 0.0138). Figure 3 and Table 1 indicate that the University of Delaware has published the most studies and has conducted strong scientific research in the study of PA intervention in ASD. The University of Delaware, University of Toronto, and Old Dominion University have formed 3 cooperation networks. Furthermore, the research institute formed a cooperative subnet with a size of 5 from 2015 to 2020. The Old Dominion University was the institution with the strongest centrality, reaching 0.29. The research institution formed a core partner in 2017 with a scale of 14. The highest ranked by Sigma ($\sum$) was the University of Massachusetts, reaching 1.58.

Overall, the network size of the PA intervention in ASD research is small, the connection density is low, and most of the cooperation is mainly intra-regional cooperation. Consider, for example, the University of Delaware, the University of Florida, the University of Virginia, McMaster University, Oregon State University, and Texas Woman's University, there is a high density of intra-regional cooperation between universities in the United States. Similarly, the Chinese University of Hong Kong, the Education University of Hong Kong, Shenzhen University, and National Cheng Kung University in China have a high density of intra-regional cooperation at the core. After 2016, the overall density of the institutional cooperation network in the field of PA intervention increased, forming

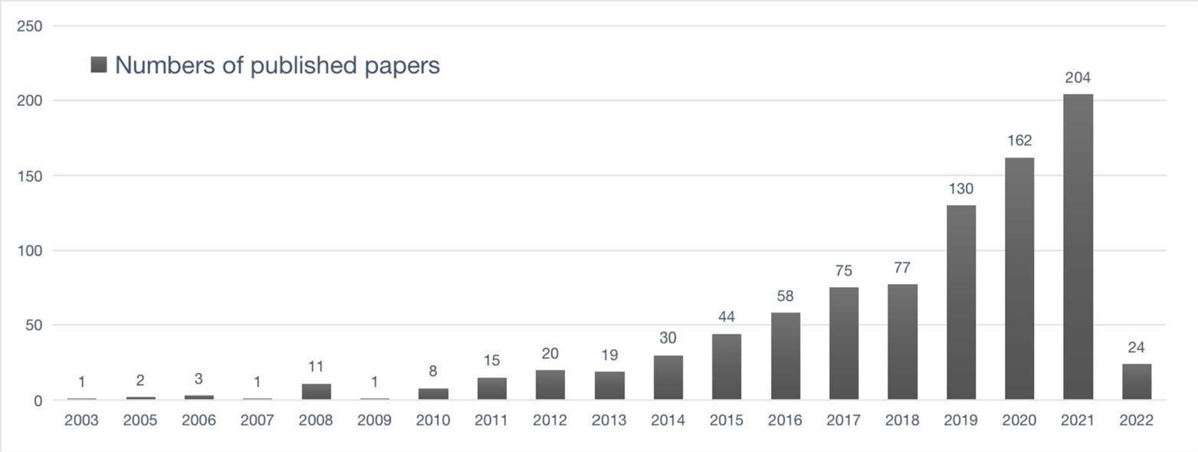

FIGURE 2
Publishing trend in the area of PA intervention for ASD (1 January 2003 to 1 March 2022).

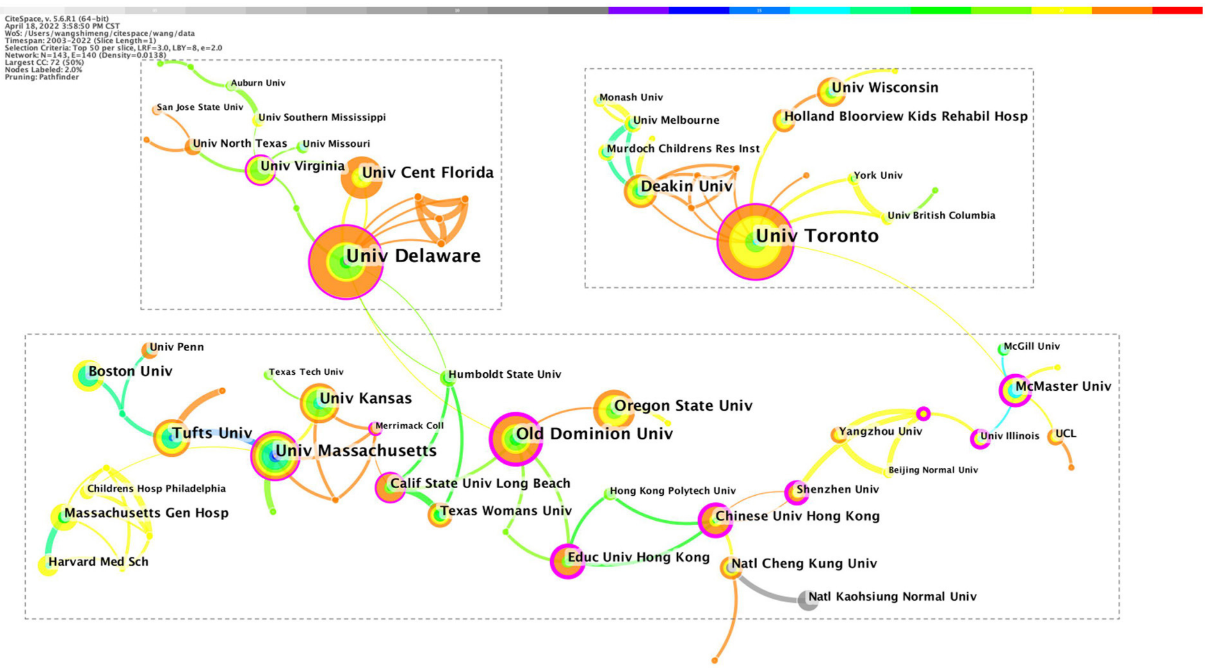

FIGURE 3
Co-institutions' network (2003–2022). The color of the circle represents when the article was published. The larger the node diameter, the more studies institutions have published. The thicker the line between the nodes, the closer the two institutions work together.

a large subnet, and the degree of cooperation was greatly improved, and cross-regional cooperation also appeared, such as a collaboration between the University of Toronto, Deakin University, University College London, McMaster University, and Yangzhou University. In addition, observing the overall high-frequency issuing agencies, Australia, North America, and Europe are more frequent, the remaining continents are small, and the cooperation density is also small. It can also be concluded that there is still a large space for cooperation between local institutions, and it is necessary to establish a more in-depth cooperative relationship of research institutions to promote the development of PA intervention in ASD research.

Co-author analysis

By analyzing the author, the cooperative relationship with others could be investigated. We ran CiteSpace, generating networks as usual: 2003–2022; Slice length: 1 year; Select the node type: Author; Top N = 50; Selection Criteria Thresholding (c, cc): 1, 1; and Choice: Pathfinder and Pruning the merged network, and other parameter settings were likely to institutions. This study found knowledge mapping of the co-author with N = 129 and E = 165 (density = 0.02). Figure 4 shows the high density of author cooperation in the field of PA intervention in ASD, such as the cooperation network centered on Sean Healy, Carol Curtin, Justin A Haegele, Jeanette M Garcia, Óscar Chiva-Bartoll, Chieyu Pan, and Aiguo Chen.

Figure 4 and Table 2 show that Sean Healy's issued quantity in this field, was the highest, reaching 3.62, and an H-index was 17. His Research Topics mainly focus on increasing PA among youth with ASD and improving the motor skills of youth with developmental disabilities. The H-index of the second Carol Curtin reached 29, and it cited a total of 1,052 times; the research area is the prevalence of obesity in disabled populations, weight loss and PA interventions for adolescents with ID and autism, and observational studies on PA, dietary patterns, and/or obesity in children with various developmental disabilities. Justin A Haegele ranked third with an H-index of 28 and 3,054 citations on the interdisciplinary field of adapted PA, with a primary interest in examining how individuals with disabilities, more specifically those with visual impairments or ASD, experience PA participation. Jeanette M Garcia, the fourth most published author, had an H-index of 18 and 1,442 citations. Research fields mainly focus on three themes, namely, developing interventions to promote healthy behaviors in youth with ASD, measurement of PA and sleep quality in underserved populations, and community-based participatory

TABLE 1 Top 10 institution published analysis (2003–2022).

Rank	Institution	Freq	Centrality	Sigma (∑)
1	University of Delaware	21	0.18	1.00
2	University of Toronto	21	0.18	1.00
3	University of Massachusetts	14	0.15	1.58
4	Old Dominion University	14	0.29	1.00
5	University of Florida	12	0.05	1.00
6	Kansas State University	12	0.01	1.00
7	Oregon State University	12	0.01	1.00
8	Tufts University	11	0.05	1.00
9	Deakin University	10	0.05	1.00
10	Univ Wisconsin	9	0.01	1.00

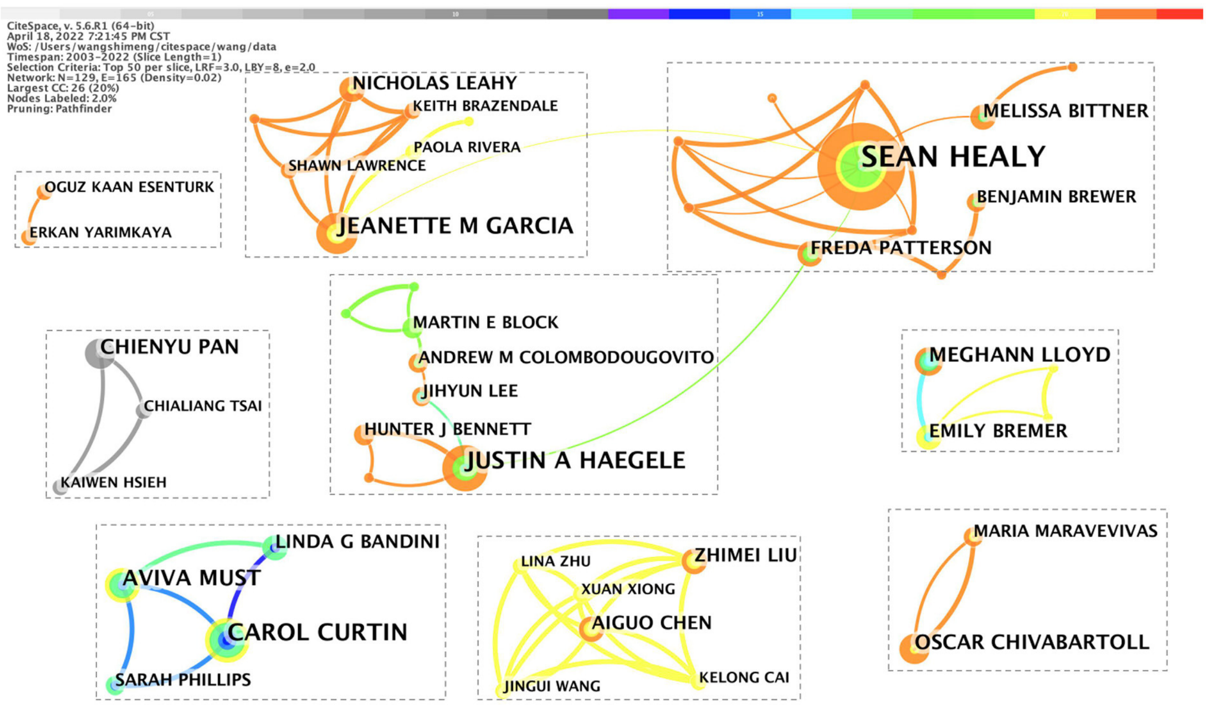

FIGURE 4
Co-authorship network (1 January 2003 to 1 March 2022). The color of the line represents the time the co-authors worked together. The larger the node diameter, the more studies the author has collaborated to publish. The thicker the line between the two authors.

TABLE 2 Co-authorship and researcher's academic information (2003–2022).

No.	Author	Freq	Burst	H-Index	Sum of cited	Research area
1	Sean Healy	17	3.62	17	1,052	Disability, autism spectrum disorder, health behaviors, physical activity, 24-h activity cycle, mixed-methods research
2	Carol Curtin	9	3.22	29	5,202	Developmental disabilities, ADHD, autism, nutrition, health promotion
3	Justin A Haegele	9	0	28	3,054	Adapted physical education, adapted physical, activity, disability, autism spectrum disorder, diversity and inclusion
4	Jeanette M Garcia	8	0	18	1,442	Autism spectrum disorder, physical activity, social/emotional/behavioral disorders
5	Óscar Chiva-Bartoll	6	0	20	1,515	Physical education, transformative pedagogy, service-learning, and teacher education

Burst refers to the specific time during which a sudden change in frequency occurs.
Sigma measures a combination of structural and temporal characteristics of nodes.
Data of H-Index, Sum of Cited, Research Area from Google Scholar.

TABLE 3 Subjects of keyword co-occurrence analysis (2003–2022).

No.	Keyword	Freq	Centrality	No.	Keyword	Freq	Centrality
1	Autism spectrum disorder	398	0.09	11	Young Children	72	0.00
2	Physical activity	354	0.05	12	Disability	65	0.33
3	Children	312	0.22	13	Health	44	0.20
4	Adolescent	290	0.10	14	Prevalence	35	0.21
5	Autism	229	0.11	15	Youth	22	0.07
6	Exercise	155	0.10	16	Motor Skill	16	0.39
7	Intervention	114	0.13	17	Adult	15	0.00
8	Spectrum disorder	113	0.09	18	Individual	13	0.22
9	Obesity	101	0.02	19	Participation	13	0.22
10	Behavior	83	0.02	20	Asperger syndrome	7	0.12

research. Óscar Chiva-Bartoll, the fifth most published author, had an H-index of 20 and citations of 1,515. His research focuses on pedagogy and philosophy of sports and methodological innovation in physics Education. All of the above scholars have made great contributions to the area of PA intervention in ASD.

Keyword analysis

Keyword co-occurrence analysis

The higher the frequency of the occurrence of keywords, the higher the probability of the keyword appearing in the research field, then the direction involved in the keyword may be more concerned by scholars, and the more likely it is that it is a hot issue in research. Table 3 shows that keyword frequency analysis helps clarify the research trends on PA intervention in ASD. PA and ASD were relatively high with frequencies of more than 350 times, because the above keywords are one of the important search terms for data sources, and they appear most frequently.

Combined with keyword frequency, children, adolescents, exercise, intervention, and obesity were relatively high with frequencies over 100 times. It shows that these keywords are more concerned by scholars in this field, reflecting that the research direction related to these keywords is the core research content of the PA intervention in ASD research field, and the study finds that PA interventions and PA in children and adolescents with ASD improve symptoms such as stereotyped behavior and motor function in patients with ASD, as well as reducing childhood obesity rates and improving quality of life may be an important research direction in this field. In addition, inconsistencies in centrality and frequency were also found in this study, such as motor skill, prevalence, individual, participant disability, and other keywords with higher centrality but lower frequency. It reflects that although these research contents have an important bridging role in the research hotspots in this field, the degree of attention needs to be strengthened.

Keyword cluster analysis

The CiteSpace generated a network as usual: 2003–2022; Slice length: 1 year; Select the node type: Keyword; Top N = 10; and Pruning choice: Pathfinder, Pruning

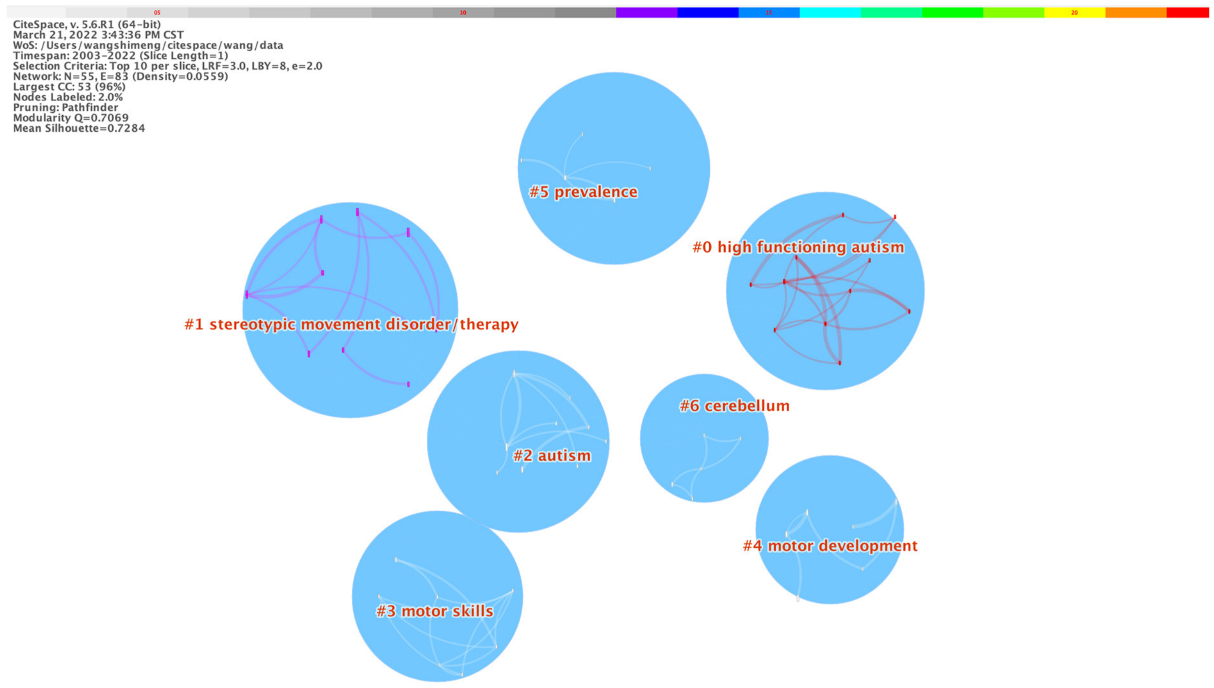

FIGURE 5
A landscape view of keyword cluster analysis generated by Top N = 10 per slice from 1 January 2003 to 1 March 2022.

TABLE 4 Subjects of cluster analysis (2003–2022).

Clusters		Silhouette	Size	Log-likelihood (LLR)
#0	High functioning autism	0.926	11	Antecedent exercise, mouse model, gene, high functioning autism, computer science, program, individual, physical exercise, skill, activity pattern, mutation
#1	Stereotypic movement disorder/therapy	0.921	10	Student, youth, exercise, physical activity, stereotypic behavior, adolescent, autism spectrum disorder, health, adult, participation
#2	Autism	1	9	Stress, acquisition, meta, system, social behavior, children, asperger syndrome, spectrum disorder
#3	Motor Skills	0.95	7	Physical activity, meta-analysis, postural control, motor skill, intellectual disability, barrier, developmental disability
#4	Motor development	0.956	4	Behavior, environment, age, disability, intervention, young children
#5	Prevalence	0.858	5	Prevalence, psychiatric disorder, obesity, overweight, spectrum
#6	Cerebellum	0.944	5	Efficacy, asd, academic achievement, fitness, inhibitory control

sliced networks, and Pruning the merged network. Given the co-occurrence of keywords, the nodes were revised, and the log-likelihood (LLR) algorithm was adopted for clustering calculation. The visualization map obtained in which N = 55 and E = 83 (density = 0.0559), the Modularity Q score was 0.7069, and the Mean Silhouette score was 0.7284, as presented in Figure 5. There was a total of 7 clusters (e.g., #0 high functioning autism, #1 stereotypic movement disorder/therapy, #2 autism, #3 motor skill, #4 motor development, #5 prevalence, and #6 cerebellum), as shown in Figure 5 and Table 4.

Clusters #0 high functioning autism and #2 autism: It is a high-functioning ASD group, as a class of disorders with higher IQ and function in ASD and milder autism symptoms; because it has obvious PA intervention effect, it is easier to integrate into the general population. It has become the preferred target for most researchers to carry out autism PA interventions (Kosari et al., 2012; Keyhani and Kosari, 2015; Ferreira et al., 2018). All patients with Asperger's syndrome or high-functioning ASD were subjected to social skills or problem behaviors, and the results were remarkable. In addition, mouse models, m gene, and meta as one of the keywords of #0 and #2 clustering have attracted the attention of the academic community in recent years. ASD is associated with genetic factors for the first time by Korvatska et al. (2002). PLD2, PLD5, PCDH10, CDH8, MET, and CNTN3 play a role in axon growth. SHANK3 and CNTNAP2 (De Rubeis et al., 2014; Otazu et al., 2021) are also involved in synaptic development. These genes are in cell adhesion, ubiquitination and GTPase/RAS signal, and other pathways. Cell adhesion pathways will affect axon guidance and synapse formation. The ubiquitin pathway affects dendritic spines and postsynaptic dense matter development. Some important abnormal gene expressions cause changes in the related pathways that affected neuronal development, structure, and function, furthermore, affecting the cortical pattern of neural circuitry may ultimately lead to the occurrence of ASD (Holt and Monaco, 2011). Therefore, based on the behavioral detection method of mouse models, scholars have conducted a series of tests on the intervention of PA in patients with ASD, including detecting learning and social interaction. Stereotypes, memory, and anxiety, provide more scientific evidence for the effect of PA intervention on ASD. Developments in the field of research must be accompanied by scientific and objective evidence, which relies on a large number of high-quality randomized controlled trials as well as meta-analyses of randomized controlled trials. Therefore, research methods, such as Meta, are also hotspots in the current research field of PA intervention in ASD, which provide important tools for accurate and efficient analysis of massive data and verification of the validity of intervention prescriptions.

Cluster #1 stereotypic movement disorder/therapy: Stereotyped behavior is a major feature of patients with ASD in all groups, manifested as aimless repetition of single actions, which seriously affects the acquisition of functional behaviors and social skills in patients with ASD, and easily leads to self-harm, emotional, and other problems. Interventions in stereotyped behavior are significant for the ASD research field. In this regard, scholars have conducted a series of studies on the effect of PA intervention on stereotyped behavior in patients with ASD based on brain imaging technology (Sorensen and Zarrett, 2014). Numerous studies have shown that PA has become an effective means of improving stereotyped behavior in patients with ASD, such as the study of Minoei et al. (2015) to intervene in ASD through horseback riding. Significant improvements have been observed in stereotyped behavior in children with ASD. The effectiveness of PA interventions on children with ASD has also demonstrated in the meta-analysis of Teh et al. (2021), arguing that exercise interventions are an evidence-based and sustainable way to improve stereotyped behavior in children with autism. Therefore, both the initial exploration of autism exercise intervention 40 years ago and the study using a more rigorous experimental design today have demonstrated the positive effect of physical exercise in improving repetitive stereotyped behaviors in children with autism, which suggests that moderate and large-intensity exercise may be better.

Clusters #3 motor skill, #4 motor development, and #5 prevalence: The development of motor function in patients with ASD is highly correlated with their language, cognitive, and social development abilities. Studies have found that regardless of the IQ level of patients with ASD, there are a variety of motor function defects, including fine movements, coarse movements, postural control, imitation, or operation. Motor deficits limit social activity, affect the development of language, behavioral, and cognitive function in people with ASD, and increase ASD with long-term decreased levels of PA risk rates for overweight and obesity in patients (Healy et al., 2018). Scholars examined the evidence of the effectiveness of PA interventions in children with autism and found that increasing PA in children and adolescents with ASD improved body mass index (BMI) and physical health, effectively alleviating their obesity rates and prevalence of ASD (Craig et al., 2021). Therefore, it can be learned that the main research content of the current research field of PA intervention on ASD motor function is oriented to the development of the motor function, reducing the risk rate of all diseases caused by motor function defects. Scientific evidence is added to the study of PA intervention in the auricular function of ASD.

Cluster #6 cerebellum: From the perspective of the role of PA in promoting the development of the cerebellum in individuals with ASD, studies have shown that individuals need the participation of the cerebellum in the process of motor control and movement; in addition, the cerebellum can also help individuals obtain and identify sensory information and has the function of coordinating muscle movement and maintaining balance in the body (Desmond and Fiez, 1998). Despite the above functions of the cerebellum, unfortunately, individuals with ASD have defects in cerebellar tissue. For example, in 95% of individuals with ASD, the cerebellum develops malformations (Abu-Elneel et al., 2008). In addition, there was developmental insufficiency in the posterior cerebellar worms and hemispheres in individuals as well as loss of Purkinje and granulocytes (Fatemi et al., 2012). Based on observations of individuals with ASDs, combined with an analysis of cerebellar function, it can be seen that cerebellar abnormalities may be a factor explaining the causes of autism. It is well-known that most exercise programs require the cortex involvement of vision, hearing, and proprioception, all of which are related to the function of the cerebellum. Therefore, it might be considered that the PA intervention is precise because the cerebellum of the individual with ASD is fully stimulated and developed so that the level of motor skills can be improved, improving their social communication skills. Clinical practice confirms that exercise promotes cerebellar neurogenesis, improves cerebellar mitochondrial function, reduces oxidative stress (Marques-Aleixo et al., 2015), and

TABLE 5 Seven keywords with the strongest citation bursts (2003–2022).

Keywords	Year	Strength	Begin	End	2003-2022
Skill	2003	4.1269	2008	2012	
Youth	2003	4.4705	2008	2014	
Participation	2003	6.7935	2010	2015	
Asperger syndrome	2003	4.4041	2010	2012	
Prevalence	2003	4.2786	2013	2016	
meta	2003	10.9935	2017	2020	
Sedentary behavior	2003	3.3561	2020	2022	

–: shows which period the citation burst is the strongest. For instance, the Skill has the longest period of burst from 2008 to 2012.

enhances the anti-apoptotic effect of neurons in the cerebellum (Seo et al., 2013).

Keyword burst analysis

To obtain the research frontier and development trend of PA intervention on ASD, the strongest keywords cited in the literature were analyzed. Keyword burst refers to keywords appearing suddenly in a short period or which usage frequency increases sharply. Overall, it reveals the evolution of the Research Topic in different periods. In this study, 7 keywords highlighted by citations are obtained through analysis, as listed in Table 5.

According to Table 5, no hot keywords have been identified in the field of research on PA interventions for ASD during the period of 2003–2008. Since 2008, skill and teen keywords have received widespread attention from scholars. Skill is an important object of PA intervention for ASD such as social skills and motor skills. The study found that overall motor skill scores were significantly lower in children with ASD compared to developing normal children, and social skills scores in children with severe movement impairment were significantly lower than in mild children (Green et al., 2009). Pan (2011) demonstrated in an experimental study that PA has a certain role in promoting water sports skills in children with ASD. Healy et al. (2018) also showed in a meta-analysis that PA has a positive impact on proactive skills, locomotor skills, and skill-related fitness. Since 2010, the key words Participation and Asperger syndrome have attracted wide attention from scholars. Asperger's syndrome is one of the syndromes of ASD, but its symptoms are mild compared to autism. Patients with Asperger's syndrome have better intelligence and language expression than those with autism but have some difficulties in social interaction. Borremans et al. (2010) compared the physical fitness and PA of ordinary adolescents with Asperger's syndrome and found balance, coordination, and coordination among adolescents with Asperger's syndrome. Abilities such as flexibility are lower than those of normal adolescents. As the intervention effect of Asperger's syndrome subjects is large, it has become the preferred object for most researchers to carry out autism PA intervention and has also become a research hotspot. Between 2013 and 2016, prevalence became a research hotspot in the field of PA interventions in ASD, and to this day, according to the Centers for Disease Control and Prevention, the prevalence of ASD has increased from 2 in 10,000 to 1 in 54 over the past 20 years (Maenner et al., 2020). Not only the prevalence of ASD but also the rate of obesity due to ASD symptoms has continued to rise. Studies have found that PA has an improving effect on the motor skills of ASD, which greatly reduces the obesity rate of patients with ASD. Over the past decade, experimental studies on PA interventions for ASD have gradually increased; however, developments in the field of research must obtain scientific and objective evidence, which relies on a large number of high-quality randomized controlled trials as well as meta-analyses of randomized controlled trials. Therefore, for the period of 2017–2020, research methods such as systematic review and meta-analysis are also hotspots in the field of PA intervention in ASD research, which also indicates that the research methods in this research field are accurate and efficient analysis of massive data. Validating the effectiveness of intervention prescriptions provides an important tool. In addition, inconsistencies in centrality and frequency were also found in this study, such as *de novo* syndrome, intellectual disability, and other keywords with higher centrality but lower frequency. It reflects that although these research contents have an important bridging role in the research hotspots in this field, the degree of attention needs to be strengthened. During 2020 to 2022, sedentary behavior became a hot keyword. With the development of the society, the application of electronic products is more and more widely, greatly influenced people's life. The popularity of electronic products reduces the time of physical activity of children with ASD, and increases the sedentary behavior of children with ASD. Studies have shown that PA can significantly improve sedentary behavior in children with ASD (Thompson et al., 2022). Therefore, the relationship between ASD children and Screen Time may be a new trend in future research on sedentary behavior.

Conclusion

This study systematically analyzed the research literature in the field of PA intervention in ASD from 1 January 2003 to 1 March 2022, using bibliometric analysis and visual analysis. The results are summarized as follows. First, the literature on PA interventions focused on ASD research shows a growing trend. It is speculated that the literature in this field will continue to grow for some time in future; in this field, the leading institution in this field is the University of Delaware; many authors have formed a network of collaborators in the field, such as Sean Healy and Carol Curtin. Second, the focus of this research area mainly includes PA interventions for children and adolescents with ASD and PA to improve symptoms such as stereotyped behaviors and motor function in patients with ASD as well as to reduce childhood obesity rates and improve quality of life of PA intervention in ASD. Third, the hotspot analysis of PA intervention in ASD research found skill, youth, prevalence, and meta-analysis systematic reviews. It is the long-term concern and focus of researchers.

In summary, as the current research status is only of short term, it is not possible to verify the long-term effect. It is a future trend to explore the long-term effects of PA interventions on ASD and to bring the best rehabilitation means to patients with ASD. Moreover, with the rapid development and mature application of brain imaging technology, brain imaging technology has become an important means to explore the underlying neural mechanisms of ASD psychology and behavior and to reveal the structure and functional characteristics of the human brain. Using brain imaging technology to analyze the mechanism of PA intervention for ASD, conducting more studies to replicate and expand the existing findings, testing the sustainability of these benefits for children with autism, and constructing a multidimensional exercise integrated intervention model are the main directions of future research in this field.

Limitation

In this study, the CiteSpace software was used to analyze current studies on PA intervention in ASD. It provides some thinking for scholars in the field of ASD to have a comprehensive understanding of the characteristics, hotspots, and development trends of the current research field and to explore intervention methods. However, there are some limitations to this study. For example, CiteSpace cannot process documents in multiple databases at the same time, and only the documents in the WoS database can be processed. Moreover, the literature of research and analysis in the English language may cause the conclusion to service because of a lack of relevant literature materials. Therefore, future research should consider analyzing a variety of databases, and multiple languages, to increase research conclusions.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding author/s.

Author contributions

AC and SW: conceptualization. SW and DC: methodology, writing—original draft preparation, investigation, data curation, and visualization. SK, AC, and IY: writing—review and editing. AC: funding acquisition. All authors have read and agreed to the published version of the manuscript.

Funding

This research was funded by the National Natural Science Foundation of China [Grant number 31771243].

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fnhum.2022.926346/full#supplementary-material

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TYPE Original Research
PUBLISHED 12 August 2022
DOI 10.3389/fnhum.2022.910624

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OPEN ACCESS

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SPECIALTY SECTION
This article was submitted to Cognitive Neuroscience, a section of the journal Frontiers in Human Neuroscience

RECEIVED 01 April 2022
ACCEPTED 18 July 2022
PUBLISHED 12 August 2022

CITATION
Cui J, Li L and Dong C (2022) The associations between specific-type sedentary behaviors and cognitive flexibility in adolescents.
Front. Hum. Neurosci. 16:910624.
doi: 10.3389/fnhum.2022.910624

The associations between specific-type sedentary behaviors and cognitive flexibility in adolescents

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Background: The prevalence of sedentary behavior in adolescents has aroused social attention. The association between sedentary behavior and cognitive flexibility remains unclear, and it may vary depending on the type of sedentary behavior. This study aimed to investigate the associations between specific-type sedentary behaviors and cognitive flexibility in adolescents.

Method: A total of 700 Chinese adolescents aged 10–15 years were recruited. The self-report questionnaire was used to assess total sedentary time, recreational screen-based sedentary time, and educational sedentary time. The More-odd shifting task was used to assess cognitive flexibility.

Results: The correlation analysis showed that recreational screen-based sedentary time was negatively correlated with cognitive flexibility, whereas educational sedentary time was positively correlated with cognitive flexibility. The regression analysis also further revealed that a significantly negative association between recreational screen-based sedentary time and cognitive flexibility, while a significantly positive association existed between educational sedentary time and cognitive flexibility.

Conclusion: The findings shown that the association between recreational screen-based sedentary behavior and cognitive flexibility differs from educational sedentary behavior in adolescents, providing new ideas for a more comprehensive understanding of the association between sedentary behavior and cognitive flexibility in adolescents.

KEYWORDS

cognitive flexibility, executive function, sedentary behavior, recreational screen-based sedentary behavior, educational sedentary behavior, adolescents

Introduction

Sedentary behavior in children and adolescents has become a global issue, attracting the attention of governments and health organizations worldwide (Graf et al., 2017; Zhang et al., 2017; World Health Organization, 2020). Sedentary behavior, distinct from physical inactivity (Ng and Popkin, 2012), is defined as any waking behavior characterized by an energy expenditure ≤1.5 metabolic equivalents while sitting, reclining, or lying (Tremblay et al., 2017). Sedentary behavior has been related to a variety of adverse health outcomes in recent years (Carson et al., 2016; Van Ekris et al., 2016), including obesity (Chen et al., 2016), increased all-cause mortality (Ekelund et al., 2019), and cardiovascular disease (Vaisto et al., 2019), implying that it is the new and major risk factor for children's and adolescents' health (Owen et al., 2020). Similarly, the negative impact of sedentary behavior may be found in the cognitive dimension (Carson et al., 2015; Falck et al., 2017). The executive function, a higher-order cognitive process, becomes the center of attention. Executive function refers to a set of top-down mental processes required for goal-directed behaviors and is linked to physical and psychological well-being as well as academic achievement in children and adolescents (Diamond, 2013). Surprisingly, the associations between sedentary behavior and executive function in children and adolescents are not well understood (Li et al., 2022). The findings of existing studies are mixed. Some studies identified a negative association between sedentary behavior and executive function (Van der Niet et al., 2015; Zeng et al., 2021), while others showed a positive association (Aadland et al., 2017; Wickel, 2017), and yet another reported no association (Mora-Gonzalez et al., 2019).

The type of sedentary behavior may be one of the major explanations for the inconsistent results of the existing studies. Sedentary behavior can be classified into several types based on the activity's content and purpose, such as recreational screen-based sedentary behavior (i.e., watching TV or playing computer), educational sedentary behavior (i.e., doing homework), and so on (Hardy et al., 2007). In this field, recreational screen-based sedentary behavior has received the most attention. According to the review study, recreational screen-based sedentary behavior may be detrimental to adolescents' executive function (Li et al., 2022). Compared to children and adolescents in other countries, Chinese children and adolescents devote more time to educational sedentary activities (i.e., reading, writing, or drawing; Duan et al., 2015; Guo et al., 2017). More importantly, a study found that sedentary time spent doing homework at age 7 years was positively associated with cognition at age 11 years, whereas sedentary time spent watching television was negatively associated with cognition, although the association was attenuated to the null after controlling for baseline cognition (Aggio et al., 2016), indicating that the type of sedentary behavior may be an important factor in understanding the association between sedentary behavior and cognition in adolescents. However, existing research tends to focus on total sedentary time rather than specific sedentary behaviors (Wickel, 2017; Mora-Gonzalez et al., 2019; Santiago-Rodriguez et al., 2022). More research is needed to build on the growing body of evidence linking type-specific sedentary behaviors (Owen et al., 2020), particularly recreational screen-based sedentary behavior and educational sedentary behavior.

In addition, it is well-known to all that executive function includes inhibitory control, working memory, and cognitive flexibility (Duncan et al., 1997; Miyake et al., 2000). Total sedentary time measured with a hip-mounted accelerometer was associated with poor inhibition but not working memory and cognitive flexibility (Van der Niet et al., 2015), implying that the effects of sedentary behavior on three core components of executive function may differ. More studies often viewed executive function as a single structure or concentrated on inhibitory control and working memory (López-Vicente et al., 2017; Horowitz-Kraus et al., 2021), while few explored the association between sedentary behavior and cognitive flexibility in adolescents. Cognitive flexibility is defined as the ability to adjust one's thoughts and behaviors in response to changing circumstances and goals (Garon et al., 2008), and it could be developed into late childhood (Chevalier et al., 2012). Cognitive flexibility, due to its complex structure, which includes inhibitory control and working memory, is likely to act as a requirement for the use of more cognitively demanding strategies in children's lives and studies (Richter and Yeung, 2012; Stokes et al., 2013; Hanks and Summerfield, 2017). Therefore, it is critical to explore the association between sedentary behavior and cognitive flexibility in adolescents.

Hence, in contrast to the previous work that focused solely on sedentary time, this current study investigates the associations between specific-type sedentary behaviors and cognitive flexibility in adolescents, examining whether the association between sedentary behavior and cognitive flexibility in adolescents varies by type. Given the high prevalence of recreational screen-based and educational sedentary behaviors in Chinese adolescents (Duan et al., 2015; Guo et al., 2017), this study investigates respectively the associations between total sedentary time, recreational screen-based sedentary behavior, educational sedentary behavior, and cognitive flexibility in adolescents. It was hypothesized that the association between recreational screen-based sedentary behavior and cognitive flexibility in adolescents would differ from the association between educational sedentary behavior and cognitive flexibility.

Materials and methods

Participants

In the current study, 700 healthy adolescents aged 10–15 years were initially recruited in China's urban areas. The predetermined inclusion criteria were as follows: (1) right-handedness; (2) no psychotropic drug use; (3) no mental or physical disability; (4) normal or corrected-to-normal vision; and (5) no emotional or behavioral problems. The Strength and Difficulty Questionnaire (child version; SDQ) with good reliability and validity was used to assess adolescents' emotional problems, conduct problems, hyper-activity-inattention, peer problems, and prosocial behavior to ensure they had no emotional or behavioral problems (Goodman, 2001). This study excluded adolescents with SDQ scores greater than 15. Finally, data from 630 adolescents (329 boys) were included in the final analysis after excluding participants with missing information about sedentary behavior or cognitive flexibility, as well as those who did not meet the inclusion criteria. The study protocol was approved by the Institutional Review Board of the East China Normal University and all study procedures met the guideline of the Declaration of Helsinki (No. HR047-2018). After completing the entire experiment, each participant signed an informed consent and received a payment of 50 RMB.

Procedures

First, self-administered questionnaires were used to collect socio-demographic information (age, sex, grade, and ethnicity). The height and body weight of adolescents were measured using a standardized height measure and scale, with the participants standing bare feet and wearing light clothing. The body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared (BMI= weight (kg) ÷ height $(m)^2$). To ensure the accuracy and reliability of the study data, researchers will introduce the questionnaire items in detail, as well as the regulations and operation steps of the cognitive flexibility task for adolescents, prior to the formal test.

Second, under the supervision of a teacher and a researcher, all participants carefully fill out the questionnaires in a clear and calm classroom. To ensure that participants complete these questionnaires honestly and in accordance with their actual situation, the researcher declares before the questionnaires begin that they have no bearing on academic performance.

Finally, all participants complete the More-odd shifting task in a clear and quiet computer classroom. Before the test, the researcher instructs participants to respond to the task as quickly as possible by pressing a button.

Sedentary behavior

Adolescents reported total sedentary time, recreational screen-based sedentary time, and educational sedentary time using a questionnaire adapted from the Adolescent Sedentary Activities Questionnaire (ASAQ) developed by Hardy et al. (2007). In Chinese children and adolescents, the Chinese vision of ASAQ has good internal consistency (overall Cronbach' α Coefficient = 0.729) and construct validity (Guo, 2016). This questionnaire also has acceptable test-retest reliability (r = 0.192–0.815) for participants in this study. Participants were asked to think about a typical week and report how much time they usually spent on all sedentary activities before and after school on each weekday and weekend. The total sedentary time was calculated by averaging the time spent each day on all sedentary activities. The recreational screen-based sedentary time was calculated using the average time spent on four of all sedentary activities for entertainment (watching television/videos/DVDs and movies, and playing computers/Ipad/phone). The educational sedentary time was calculated using the average time spent on three of all sedentary activities for learning (study with/without computer, and tutoring).

Physical activity

Physical activity was measured using the Physical Activity Questionnaire for older children and adolescents (PAQ), which was developed by Kowalski et al. (2004) and updated by Guo (2016). This questionnaire has been validated in China for use with children and adolescents, and it has adequate reliability (Cronbach's α = 0.82) and validity (Guo, 2016). This questionnaire was divided into three sections. The first section of the questionnaire was intended to determine how frequently adolescents participate in various sports such as skipping rope and basketball; the second section was intended to determine the adolescents' physical activity during various periods such as after school and physical education; and the third section was intended to determine the average frequency of physical activity over the previous 7 days. Finally, the average of three sections was calculated and used to describe adolescents' level of physical activity. The higher the score, the greater the level of physical activity there is. The level of physical activity was classified as high (the score > 3), medium (3 ≥ the score > 2), and low (the score ≤ 2; Chen et al., 2008).

Cognitive flexibility

Cognitive flexibility was measured using the More-odd shifting task (Chen et al., 2014). The More-odd shifting task consists of a series of numeric digits displayed in the center of the screen, ranging from either 1 to 4 or 6 to 9. All digits were displayed for 1,500 ms, and the ISI was set to 1,000 ms. There were three types of blocks, each of which ran twice. For A block in which the digits were printed in white, participants were required to indicate whether the presented digit was larger than or less than five by pressing the "C" or the "M" key respectively. For B block in which the digits were printed in red, participants were asked to indicate whether the presented digit was odd or even by pressing the "C" or the "M" key respectively. For C block included both A- and B-type trials (16 trials each), with the trials switching from one to the other every two trials. Participants were required to press the "C" or "M" key to identify whether the digit was larger or less than five when the digit was presented in white, and whether the digit was odd or even when the digit was presented in red. The experiment lasted 480 s in total. The accuracy of the heterogeneous (C blocks), the accuracy of the homogeneous (A and B blocks) blocks, as well as the difference in reaction time between the heterogeneous and homogeneous blocks, were recorded and utilized to develop cognitive flexibility indexes.

Statistical analysis

The data were analyzed using statistical software (SPSS Version 26.0, IBM Corporation, Somers, NY, USA), with a significance level accepted as $p < 0.05$. All descriptive data (age, height, weight, BMI, physical activity, sedentary behavior, and cognitive flexibility) were reviewed and presented as mean ± SD to summarize the participants' characteristics. The Shapiro-Wilk test was used to assess the normal distribution of sedentary behavior (Shapiro and Wilk, 1965). Then, the Mann-Whitney U was used to calculate the gender difference (boys vs. girls) in sedentary behavior, and the effect size was calculated as the Cohen's d (Lenhard and Lenhard, 2016). Pearson's correlation analysis was used to assess the correlations between sedentary behavior (total sedentary time, recreational screen-based sedentary time, and educational sedentary time) and cognitive flexibility (the accuracy and difference in reaction time of the More-odd shifting task). Hierarchical linear regressions analysis was performed to evaluate respectively the association between each independent variable (total sedentary time, recreational screen-based sedentary time, and educational sedentary time) and each cognitive outcome (the accuracy of the heterogeneous blocks, the accuracy of the homogeneous blocks, the difference in the average reaction time between the heterogeneous and the homogeneous blocks in the More-odd shifting task), while adjusting for covariates (age, sex, BMI, and physical activity).

Results

Descriptive statistics analysis

The descriptive characteristics of sedentary behavior and cognitive flexibility were presented in **Table 1** and **Table 2**. In terms of total sedentary time, the average time per day was 5.753 (SD = 2.367) hours, and there was no statistically significant difference between girls and boys ($p = 0.479$). In terms of recreational screen-based sedentary behavior, the average time per day was 1.438 (SD = 1.500) hours. Furthermore, there was a minor but significant gender difference ($p < 0.049$, Cohen's $d = 0.158$), with boys spending considerably more time on recreational screen-based sedentary behavior than girls. In terms of educational sedentary behavior, the average time per day was 2.437 (SD = 1.451) hours, with no significant difference between girls and boys ($p = 0.796$). In terms of physical activity, the average score was 2.325 (SD = 0.879), indicating that adolescents' physical activity is at a medium level.

Correlation analysis

The recreational screen-based sedentary time was negatively correlated with both the accuracy of the heterogeneous ($r = -0.134$, $p = 0.001$) and homogeneous blocks ($r = -0.181$, $p < 0.0001$), but positively correlated with difference in reaction time between the heterogeneous and the homogeneous blocks ($r = 0.09$, $p = 0.023$); On weekdays, recreational screen-based sedentary time was negatively correlated with the accuracy of the heterogeneous ($r = -0.155$, $p < 0.001$) and homogeneous blocks ($r = -0.168$, $p < 0.0001$). On weekends, it was negatively correlated with the accuracy of the heterogeneous ($r = -0.082$, $p = 0.038$) and homogeneous blocks ($r = -0.166$, $p < 0.001$), while it was positively correlated with difference in reaction time between the heterogeneous and the homogeneous blocks ($r = 0.093$, $p = 0.019$).

The educational sedentary time was both positively correlated with the accuracy of the heterogeneous blocks ($r = 0.125$, $p = 0.002$) and the accuracy of the homogeneous blocks ($r = 0.127$, $p = 0.001$). On weekdays, educational sedentary time was positively correlated with the accuracy of the homogeneous blocks ($r = 0.107$, $p = 0.007$). On weekends, educational sedentary time was positively correlated with both the accuracy of the heterogeneous blocks ($r = 0.16$, $p < 0.001$) and the accuracy of the homogeneous blocks ($r = 0.115$, $p = 0.004$).

There was no correlation between total sedentary time and any of the More-odd shifting task measures ($p > 0.05$).

Regression analysis

The results of the regression analysis assessing the association between recreational screen-based sedentary time and cognitive flexibility were presented in **Table 3**. After controlling for age, sex, BMI, and physical activity, recreational screen-based sedentary time was significantly inversely related to the accuracy of heterogeneous blocks ($\beta = -0.103$, $p = 0.019$, 95% confidence interval (CI) [−0.009, −0.001]); Similarly, on weekdays, it also was significantly inversely related to the accuracy of heterogeneous blocks ($\beta = -0.127$, $p = 0.003$, 95%CI [−0.012, −0.003]).

The results of the regression analysis assessing the association between educational sedentary time and cognitive flexibility were presented in **Table 3**. After controlling for age,

TABLE 1 The descriptive characteristics of the participants' demographic and sedentary behaviors (Mean ± SD).

	All (*N* = 630)	Boys (*N* = 301)	Girls (*N* = 329)
Age (year)	12.019 ± 1.572	11.893 ± 1.546	12.134 ± 1.589
Height (m)	1.519 ± 0.129	1.518 ± 0.144	1.519 ± 0.113
Weight (kg)	45.025 ± 12.866	46.541 ± 14.528	43.638 ± 10.970
BMI (kg/m^2)	19.217 ± 3.420	19.799 ± 3.666	18.684 ± 3.089
Physical activity	2.325 ± 0.879	2.344 ± 0.880	2.308 ± 0.879
TST (h/d)	5.753 ± 2.367	5.827 ± 2.412	5.685 ± 2.327
Weekday TST (h/d)	4.746 ± 2.172	4.812 ± 2.230	4.687 ± 2.119
Weekend TST (h/d)	8.121 ± 3.631	8.222 ± 3.779	8.029 ± 3.494
SST (h/d)	1.438 ± 1.500	1.551 ± 1.610	1.336 ± 1.386
Weekday SST (h/d)	1.012 ± 1.264	1.037 ± 1.386	0.990 ± 1.143
Weekend SST (h/d)	2.494 ± 2.559	2.822 ± 2.706	2.193 ± 2.382
EST (h/d)	2.437 ± 1.451	2.500 ± 1.553	2.380 ± 1.351
Weekday EST (h/d)	2.211 ± 1.398	2.318 ± 1.533	2.113 ± 1.256
Weekend EST (h/d)	3.003 ± 2.347	2.953 ± 2.410	3.049 ± 2.290

BMI, Body Mass Index; TST, total sedentary time; SST, recreational screen-based sedentary time; EST, educational sedentary time; h/d, hour per day.

TABLE 2 The descriptive characteristics of the participants' cognitive flexibility (Mean ± SD).

	All (*N* = 630)	Boys (*N* = 301)	Girls (*N* = 329)
AB.ACC (%)	0.876 ± 0.085	0.881 ± 0.087	0.871 ± 0.083
C.ACC (%)	0.857 ± 0.075	0.861 ± 0.076	0.854 ± 0.074
Mos.RT (ms)	202.048 ± 101.189	197.116 ± 103.675	206.561 ± 98.802

AB.ACC, the accuracy of the homogeneous blocks in the More-odd shifting task; C.ACC, the accuracy of the heterogeneous blocks in the More-odd shifting task; Mos.RT, the difference in the average reaction time between the heterogeneous and the homogeneous blocks in the More-odd shifting task.

TABLE 3 Regression analysis for the associations between sedentary behaviors and cognitive flexibility (*N* = 630).

	R^2	R^2_{adj}	F_{change}	*P*	B	β	95% CI	
							lower limits	upper limits
AB.ACC								
TST	0.220	0.213	0.092	0.762	0	0.011	−0.002	0.003
SST	0.219	0.213	0.004	0.949	0	0.002	−0.004	0.004
EST	0.220	0.213	0.213	0.644	0.001	0.017	−0.003	0.005
C.ACC								
TST	0.018	0.011	0.090	0.764	0	−0.012	−0.003	0.002
SST	0.027	0.019	5.562	0.019*	−0.005	−0.103	−0.009	−0.001
EST	0.028	0.020	6.037	0.014*	0.005	0.100	0.001	0.009
Mos.RT								
TST	0.039	0.032	2.049	0.153	2.409	0.056	−0.896	5.714
SST	0.037	0.029	0.582	0.446	2.226	0.033	−3.506	7.957
EST	0.039	0.031	1.784	0.182	3.762	0.054	−1.770	9.294

TST, total sedentary time; SST, recreational screen-based sedentary time; EST, educational sedentary time; CI, confidence interval; AB.ACC, the accuracy of the homogeneous blocks in the More-odd shifting task; C.ACC, the accuracy of the heterogeneous blocks in the More-odd shifting task; Mos.RT, the difference in the average reaction time between the heterogeneous and the homogeneous blocks in the More-odd shifting task; R^2, determination coefficient of the regression; R^2adj, the adjusted R^2 from the regression analysis model; *$p < 0.05$.

sex, BMI, and physical activity, educational sedentary time was found to be significantly positively associated with the accuracy of heterogeneous blocks in the More-odd shifting tasks (β = 0.1, p = 0.014, 95% CI [0.001, 0.009]). Similarly, on weekends, it also was found to be significantly positively associated with the accuracy of heterogeneous blocks in the More-odd shifting tasks (β = 0.143, $p < 0.001$, 95% CI [0.002, 0.007]).

The results of the regression analysis assessing the association between total sedentary time and cognitive flexibility were presented in Table 3. No associations were observed between total sedentary time and any measures of the More-odd shifting task ($p > 0.05$) after controlling for age, sex, BMI, and physical activity.

Discussion

In the current study, we examined whether the association between sedentary behavior and cognitive flexibility differed by type in adolescents. We found innovatively that the association between recreational screen-based sedentary time and cognitive flexibility differs from the association between educational sedentary time and cognitive flexibility. To be specific, recreational screen-based sedentary behavior was found to be negatively associated with cognitive flexibility, whereas educational sedentary behavior was found to be positively associated with cognitive flexibility in adolescents. These findings supported our hypothesis.

Previous studies have demonstrated that recreational screen-based sedentary behavior has a negative impact on adolescents' cognition (Swing et al., 2010; Weis and Cerankosky, 2010). Furthermore, according to a recent systematic review study, screen-based sedentary behavior in children and adolescents may be negatively associated with executive function (Li et al., 2022). Our findings in this study back up previous studies and reviews by demonstrating a significantly negative association between recreational screen-based sedentary time and cognitive flexibility in adolescents, particularly on weekdays. There could be several explanations for these negative associations. First, recreational screen-based sedentary behavior (i.e., watching TV) frequently provides children and adolescents with intense and stimulating sensory experiences, leading to children spending more time on such behaviors and significantly crowding out time spent on cognitive development-promoting behaviors (i.e., do homework; Koolstra et al., 1997). Second, screen exposure may be related to inattentive symptoms (Zivan et al., 2019), slow processing of cognitive resource, and poor memory ability (Horowitz-Kraus et al., 2021), all of which can impair cognitive flexibility. Third, new neuroimaging studies have revealed that the increased recreational screen-based sedentary behavior was associated with decreased gray matter volume in the frontal lobe (Zavala-Crichton et al., 2020) and decreased fractional anisotropy in white matter tracts related to EF (Hutton et al., 2020). As we all know, the frontal lobe is an important brain area responsible for executive functions such as cognitive flexibility (Pribram, 1976).

Educational sedentary behavior is extremely common in Chinese children and adolescents, owing to increased social and cultural pressures associated with academic performance (Tudor-Locke et al., 2003; Cui et al., 2011). However, only a few studies have explored the association between educational sedentary behavior (i.e., doing homework) and cognitive function in children and adolescents (Aggio et al., 2016; Lizandra et al., 2016; Hunter et al., 2018). Building on prior studies, the current study, in greater depth, investigated the association between educational sedentary behavior and cognitive flexibility. Our findings showed that educational sedentary behavior was positively associated with cognitive flexibility in adolescents, particularly on weekends. On the one hand, these findings could be explained by the high-level cognitive engagement associated with this type of behavior. Adolescents' cognitive development can be boosted by engaging in cognitively active sedentary behavior such as reading and learning (Sweetser et al., 2012). Sedentary behaviors related to academic skills (i.e., reading and writing) have been shown to be positively associated with cognitive function (Haapala et al., 2014); on the other hand, these findings could also be explained by functional changes in the brain area that supports executive function. Evidence from brain imaging study shows that reading was found to be positively correlated with increased functional connectivity between the visual word form area and regions supporting executive function and cognitive control (i.e., inferior prefrontal gyrus; Horowitz-Kraus and Hutton, 2018).

The current study extends our understanding of the association between sedentary behavior and cognitive flexibility. These novel findings in the current study suggest that the association between recreational screen-based sedentary behavior and cognitive flexibility differs from educational sedentary behavior, and they provide preliminary evidence for the association between sedentary behavior and cognitive flexibility in adolescents varies by type. These findings also suggest that, with the exception of sedentary time, the type of sedentary behavior may have an impact on the association between sedentary behavior and cognitive flexibility, which opens up new avenues for future research. Furthermore, this study discovered that the association between sedentary behavior and cognitive flexibility differs on a weekday vs. weekends, implying that we should limit adolescents' recreational screen-based sedentary time on weekdays to guarantee healthy cognitive development. However, it is worth noting that these correlations in the current study were statistically significant but small, implying that more research is needed in the future to explore and validate these ideas.

The current study has several limitations that should be mentioned. First, the questionnaire used in this study can well investigate recreational screen-based sedentary behavior, educational sedentary behavior, and total sedentary time. This self-report questionnaire, however, may have some subjective variation. In addition, we did not recruit children from primary school (grades 1–3), because children in grades 1–3 of primary school have a low cognitive level and may not be able to accurately understand the items in these self-report questionnaires. Second, given Chinese adolescents' sedentary status, this study only surveyed recreational screen-based sedentary behavior and educational sedentary behavior. To fully understand the associations between sedentary behavior and cognitive flexibility in adolescents, researchers should investigate other types of sedentary activity (such as travel sedentary behavior and social sedentary behavior). Lastly, because this is a cross-sectional study rather than a longitudinal cohort study, it is impossible to determine the causal associations between sedentary behavior and cognitive flexibility. Clearly, longitudinal investigations will be required in future studies to explore and validate the deeper associations between sedentary activity and cognitive flexibility in adolescents.

Conclusion

In summary, our findings show that the association between recreational screen-based sedentary behavior and cognitive flexibility differs from educational sedentary behavior, providing new perspectives for fully understanding the associations between sedentary behavior and cognitive flexibility in adolescents.

Data availability statement

The original contributions presented in the study are included in the article, further inquiries can be directed to the corresponding author/s.

Ethics statement

The studies involving human participants were reviewed and approved by the Institutional Review Board of the East China Normal University and met the guideline of the Declaration of Helsinki (No. HR047-2018). Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

Author contributions

JC and LL: conceptualization, methodology, and investigation. JC, CD, and LL: formal analysis and writing—original draft. JC and CD: writing—review and editing. All authors contributed to the article and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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frontiers | Frontiers in Human Neuroscience

TYPE Original Research
PUBLISHED 12 September 2022
DOI 10.3389/fnhum.2022.960286

Modulating break types induces divergent low band EEG processes during post-break improvement: A power spectral analysis

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SPECIALTY SECTION
This article was submitted to Cognitive Neuroscience, a section of the journal Frontiers in Human Neuroscience

RECEIVED 02 June 2022
ACCEPTED 03 August 2022
PUBLISHED 12 September 2022

CITATION
Wang S, Zhu L, Gao L, Yuan J, Li G, Sun Y and Qi P (2022) Modulating break types induces divergent low band EEG processes during post-break improvement: A power spectral analysis.
Front. Hum. Neurosci. 16:960286.
doi: 10.3389/fnhum.2022.960286

Conventional wisdom suggests mid-task rest as a potential approach to relieve the time-on-task (TOT) effect while accumulating evidence indicated that acute exercise might also effectively restore mental fatigue. However, few studies have explored the neural mechanism underlying these different break types, and the results were scattered. This study provided one of the first looks at how different types of fatigue-recovery break exerted influence on the cognitive processes by evaluating the corresponding behavioral improvement and neural response (EEG power spectral) in a sustained attention task. Specifically, 19 participants performed three sessions of psychomotor vigilance tasks (PVT), with one session including a continuous 30-min PVT while the other two sessions additionally inserted a 15-min mid-task cycling and rest break, respectively. For behavioral performance, both types of break could restore objective vigilance transiently, while subjective feeling was only maintained after mid-task rest. Moreover, divergent patterns of EEG change were observed during post-break improvement. In detail, relative theta decreased and delta increased immediately after mid-task exercise, while decreased delta was found near the end of the rest-inserted task. Meanwhile, theta and delta could serve as neurological indicators to predict the reaction time change for exercise and rest intervention, respectively. In sum, our findings provided novel evidence to demonstrate divergent neural patterns following the mid-task exercise and rest intervention to counter TOT effects, which might lead to new insights into the nascent field of neuroergonomics for mental fatigue restoration.

KEYWORDS
mental fatigue recovery, time-on-task (TOT), sustained attention, EEG, power spectral density, exercise

Introduction

In contemporary society, sustaining steady attention for a long period is a challenging yet necessary cognitive process on numerous occasions (Thomson et al., 2015; Esterman and Rothlein, 2019). However, prolonged mental activities are inevitably accompanied by impaired executive control ability (Langner and Eickhoff, 2013; Thomson et al., 2015) and deteriorated performance in attention-related tasks (Boksem et al., 2006; Wascher et al., 2014), like an increased propensity for lapses/errors and slowed reaction time. Collectively, these objective declines are known as the effects of time-on-task (TOT) (Mackworth, 1948; Lim et al., 2010, 2013). TOT-altered effects have been repeatedly revealed in on-the-job lapses in industries where workers are required to work for long periods without rest, leading to lowered productivity and increased safety risks. Because of these undesirable yet preventable consequences, emerging efforts have been made to find an efficient countermeasure for the TOT effect (Helton and Russell, 2017).

As a non-invasive measurement, EEG has been widely employed in mental fatigue studies and provided several promising results (Borghini et al., 2014; Thomson et al., 2015; Helfrich and Knight, 2016; Sun et al., 2017; Gao et al., 2019). For instance, accumulating evidence suggested that increased low-band (i.e., 1–7 Hz) neural activity (Craig et al., 2012) was broadly recognized as an indication of increasing mental fatigue. In a recent meta-analysis, increased theta band (i.e., 4–7 Hz) neural activity was reported to serve as a sailent neural biomarker of mental fatigue across the frontal, central, and posterior cortical sites (Tran et al., 2020). Besides, the increase of delta (i.e., 1–4 Hz) was also repeatedly observed during mental fatigue in aircraft pilots and car drivers (Borghini et al., 2014), visual attention tasks (Ko et al., 2017), and steady-state visual evoked potential (SSVEP) experiments (Cao et al., 2014). Based on these fatigue-induced EEG findings, Clayton et al. proposed the oscillation model of sustained attention, where they postulated that frontal theta was associated with monitoring and control of cognitive processes, and increased frontomedial-theta power might manifest detection of a mismatch between current and desired levels of attention (Clayton et al., 2015). In sum, a relatively comprehensive picture pertaining to the neural characteristics of mental fatigue has been obtained. Nonetheless, only until recently, studies started to quantitatively investigate the biobehavioral performance of break-related fatigue recovery and reported mixed findings (Wascher et al., 2014; Lim et al., 2016).

Conventional wisdom suggests that mid-task rest is a potential intervention to reduce mental fatigue and burst cognitive performance. For example, Lim investigated the effect of different rest durations (i.e., 1, 5, and 10 min) on mental fatigue recovery and indicated that longer breaks were associated with better restoration of behavioral performance (Lim et al., 2016). Moreover, Helton et al. showed that during the vigilance task, participants performed better after resting than switching to a secondary task (Helton and Russell, 2015). In addition to the well-known rest intervention approach, accumulating meta-analytical evidence (Chang et al., 2012) and reviews (Pontifex et al., 2019; Tomporowski and Pesce, 2019) indicated that acute moderate-intensity exercise was effective for improving cognitive performance, especially in restoring attention (Fernandes et al., 2019). An increased physical activity level was also found to be associated with reduced subjective fatigue (Southard et al., 2015; Sonnentag, 2018). However, in comparison with those consistent findings indicating that breaks restore fatigue-related behavioral assessments, the results about their underlying neural mechanism are relatively mixed. For instance, Phipps-Nelson et al. showed that rest break did improve driving performance after fatigue, yet failed to identify any beneficial effect of rest on EEG characteristics (Phipps-Nelson et al., 2011). Besides, Lim et al. did not observe any time by condition interaction of EEG activities between successive and rest-inserted auditory oddball tasks (Lim et al., 2013). Moreover, in our recent work investigating the neural mechanism of post-exercise performance restoration, no significant difference was observed between successive task and exercise-inserted task in static dynamic functional connectivity (FC) analysis (Gao et al., 2020), and similar dynamic FC development trends were exhibited between tasks with exercise-break and rest-break (Gao et al., 2022). Generally, these scattered studies still suggested a nascent trend in the field of neuroergonomics to further uncover the divergent underlying neural mechanisms of different fatigue recovery approaches.

This research gap has been a key motivation for this study. In particular, our study investigated this undiscovered post-intervention improvement difference by comparing the neural activity change and cognitive pattern of mid-task rest and exercise. In the laboratory, tests of sustained attention have been particularly amenable for inducing the TOT effect because of their reliability and validity. Therefore, a previously validated psychomotor vigilance task (PVT) paradigm was used in this work. Specifically, a within-subject three-session design was adopted, with one session consisting of a continuous 30-min PVT while the other two sessions additionally included a 15-min mid-task rest break and a 15-min cycling break, respectively. Unlike our previous research that focused on network analysis and revealed non-significant effects (Gao et al., 2020), EEG power spectral analysis was utilized to interrogate the processes in a low-frequency band in this study, which aimed to explore how different types of fatigue-recovery break exerted influence on the cognitive processes from a new perspective. In detail, delta (1–4 Hz) and theta (4–7Hz) bands were proved to be sensitive to wakeful and sleep mental states and therefore considered a potential biomarker for the wakefulness assessment (Tran et al., 2020). We further examined the association between these brain activities and vigilance behavioral performance. Based on the reported beneficial effects of exercise (Pontifex et al., 2019) and rest (Lim et al., 2016), we hypothesized that both interventions would relieve TOT effects from a biobehavioral perspective. Based on the divergent characteristics of the two types of intervention, we further hypothesized that exercise break and rest break exerted different impacts on cognitive processes of sustained attention, which might be manifested as different spatio-spectral power activity changes.

Methods and materials

Participants

Twenty-one healthy young adults from Zhejiang University were recruited in this study *via* an online advertisement. Among them, two subjects were excluded due to data acquisition issues, and the remaining 19 subjects (male/female = 13/6, age = 22.16 ± 0.65 years) were included for the following analysis. All participants had normal or corrected-to-normal vision. None of them reported cardiovascular, cognitive disorder, color blindness, or any acute illness that might influence the cognitive task performance. Each participant was informed of the experimental protocol and potential risks through a telephone interview. They were required to get a full night of sleep (> 7 h, recorded by HUAWEI-B19 bracelet) for two continuous nights and were instructed to abstain from caffeine and alcohol and avoid vigorous physical activity for 7 h before the experiment. Those participants who failed to meet the requirements were either ruled out from the experiment or rescheduled. Upon arriving at the lab, written informed consent and Physical Activity Readiness Scale (PARS) were provided to exclude any contraindication during exercise. This study was approved by the Institutional Review Board of Zhejiang University and was carried out in compliance with the Declaration of Helsinki.

Experimental protocol

A within-subject design was adopted in this work to explore the effects of receiving different types of breaks on mental fatigue recovery, where each participant was requested to finish three sessions in a counterbalanced manner with approximate 1-week interval (Figure 1). During each session (namely, *No-Break*, *Exercise-Break,* and *Rest-Break* session, respectively), participants were required to perform a 30-min PVT with or without a break. The design of PVT was the same as in our previous studies (Gao et al., 2020). Briefly, during the test, subjects were required to monitor a red dot that appeared on the screen and responded to this stimulus by pressing the space bar as soon as possible. Intervals between trials varied randomly from 2 to 10 s (mean = 6 s).

In the *No-Break* session, participants were required to perform the PVT task continuously without a break, while during the *Rest-* or *Exercise-Break* session, participants were required to perform PVT tasks with a 15-min still sitting with eyes fixed on a black cross (namely *mid-task rest)* or cycling on a Monark 975 stationary exercise bicycle (namely *mid-task exercise*) in the middle of the tasks. Sessions were arranged at the same time of the day to eliminate the impact of circadian rhythm (Pontifex et al., 2019). The *mid-task rest* was introduced with the notion that rest breaks induced mental fatigue recovery (Lim et al., 2013; Sun et al., 2017; Qi et al., 2020), while the *mid-task exercise* corresponded to the view that the moderate-intensity exercise led to cognitive improvement (Chang et al., 2012). The intensity of the cycling break was estimated at individual-level using the following formula:

$$\text{Target HR} = (HR_{max} - HR_{rest}) \times 55{\sim}65\% + HR_{rest}$$

where HR stands for heart rate, and HR_{max} was set as 220 – age, HR_{rest} was obtained after participants resting for 5∼7 min (recorded by the Polar Vantage V). In addition, subjective feelings of mental states were assessed *via* the Short Stress State Questionnaire (SSSQ) (Helton et al., 2005; Lim et al., 2016; Qi et al., 2020) before and immediately after each session. Three minutes was determined as the length of an epoch to better illustrate the transient effect of post-break while including enough PVT trials for a stable behavioral and electrophysiological metrics estimation.

EEG recording and pre-processing

High-density continuous EEG was recorded from 64 Ag/AgCl scalp electrodes (model: Brain Products MR Plus, Germany) according to the International 10–20 system during the 30-min PVT for three sessions. The sample rate was set at 2,000 Hz with reference to the FCz. The impedance was kept below 5 kΩ during the whole data collection. In the offline analysis, a previously validated standard EEG preprocessing pipeline was adopted. Briefly, all data were down-sampled to 256 Hz, bandpass filtered into 1–40 Hz, 50 Hz notch filtered, and average re-referenced. Independent component analysis (ICA) (Jung et al., 1997) was further used to detect and eliminate artifacts (i.e., EOG and eye movements). Then for each 3-min epoch, the obtained EEG data were de-trended and segmented into 6-s trials (corresponding to the average time of one behavioral trial in the PVT). EEG data in an epoch with a voltage >100 uV was rejected (Zhao et al., 2012). For all preprocessing steps, customized codes and the EEGLab toolbox (Delorme and Makeig, 2004) were used in MATLAB 2020B.

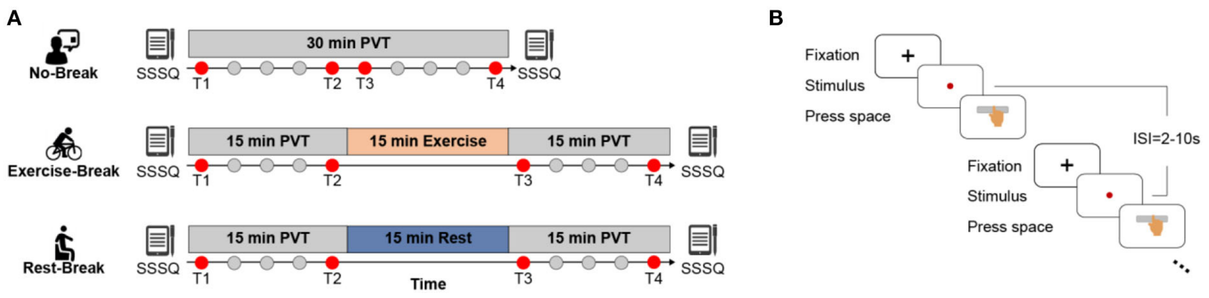


FIGURE 1
Schematic illustration of the experimental protocol. **(A)** No-Break session includes a 30-min continuous PVT task, while Exercise-Break and Rest-Break session are intervened by a 15 min mid-task exercise and mid-task rest, respectively. Of note, T1 and T4 that correspond to the first and last 3 min of each session; and T2 and T3 that represent the pre-break and post-break 3 min of each session were defined to investigate the immediate effect (T2 vs. T3) and general effect (T1 vs. T4) for post-break intervention. **(B)** The detailed paradigm of PVT task. Subjects were required to press the space bar as quickly as possible after monitoring the stimulus (red dot), with 2–10 s inter-stimulus-intervals (ISI).

Power analysis

Each 6-s EEG data trial was divided into segments using a 100% Hamming window of 1 s, then the power spectral density (PSD) was estimated by Welch's method, and specially focused on two low-frequency bands: delta band (1–4 Hz) and theta band (4–7 Hz) for their potential sensitivity toward mental states (Tran et al., 2020). For each channel, relative power (P_δ and P_θ) was estimated as the ratio of the specific band power to the total power spectral that was estimated with a frequency range of 1–40 Hz. For each 3-min epoch, averaged relative power was obtained from all included trials.

Meta-analysis suggested that spectral EEG across frontal, central, and posterior cortical regions was related to mental fatigue, and the effect size was large for the central region and moderate for the frontal and posterior regions (Tran et al., 2020). Considering these region-dependent alterations of EEG power during TOT (Craig et al., 2012; Lim et al., 2013), three bilateral clusters (corresponding to frontal, central, and parietal areas) were divided to better investigate the restorative effect of different breaks. The assignment of electrodes in each cluster is displayed in Figure 2.

Statistical analysis

Behavioral variables

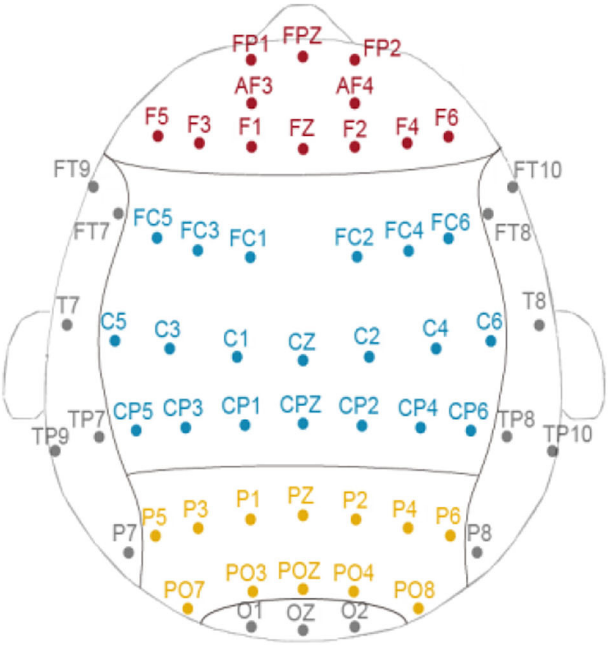
Consistent with the previous study (Gao et al., 2022), we primarily focused on the reaction time (RT) for the analysis of behavioral performance, as it was directly affected by fatigue (Dorrian et al., 2004). In detail, an RT longer than 500 ms was considered a lapse, and a RT shorter than 100 ms was considered a false alarm. Hence, only RTs between 100 and 500 ms after the stimulus onset were included in the following statistical analyses. To investigate the effectiveness of the PVT-induced TOT effect, one-way repeated-measures ANOVA for RT in ten 3-min bins was conducted in the *No-Break* session, as well as an assessment of the slope of RT. For the effect of mid-task breaks, previous evidence showed that post-break behavioral improvements were transient (Lim and Kwok, 2015; Lim et al., 2016). Therefore, we evaluated the intervention effect of breaks from two aspects: immediate and general effect. Of note, T1 and T4 correspond to the first and last 3 min of each session; and T2 and T3 represent the pre-break and post-break 3 min of each session and were defined to investigate the immediate effect (T2 vs. T3) and general effect (T1 vs. T4) for post-break intervention. Specifically, a two (Time: T2 and T3) by three (Session: *No-Break*, *Exercise-Break*, and *Rest-Break*) repeated measures two-way ANOVA on RT was adopted to explore the immediate influence of breaks, while another repeated measures two-way ANOVA with Time (T1 and T4) by Session (*No-Break*, *Exercise-Break*, and *Rest-Break*) on RT was conducted to investigate the long-lasting general effect.

Subjective feelings

As mentioned previously, the subjective feelings of participants were also assessed *via* SSSQ prior to and immediately after the PVT. Heuristically, the 24-item SSSQ could be divided into three categories: engagement, worry, and distress (Helton et al., 2005). To assess the subjective mental states before and after the tasks, a separate two (Time: Pre-session, Post-session) by three (Session: *No-Break*, *Exercise-Break,* and *Rest-Break*) repeated measures ANOVA was conducted on the SSSQ scores of each category.

EEG power

To comprehensively depict the break-related spectral changes in the low-frequency range, averaged EEG power ratio of two frequency bands (delta and theta) in the three clusters (Figure 2) was obtained. Similar to the behavioral variable, the



Clusters	Electrodes
Frontal	FP1-2,AF3-4,F1-6,Fz,FPz
Central	FC1-6,C1-6,CP1-6,Cz,CPz
Parietal	P1-6,PO3-4,PO7-8,Pz,POz

FIGURE 2
The assignment of electrodes in frontal, central, and parietal clusters.

immediate effect (i.e., T2 vs. T3) and general effect (i.e., T1 vs. T4) of the mid-task breaks were assessed through separate two by three repeated measures two-way ANOVA with Time by Session (*No-Break*, *Exercise-Break*, and *Rest-Break*). Specifically, the dependent variables were the multiband EEG power ratio in different brain clusters.

Correlation

For the frequency band displaying the significant spectral difference in the last step, the correlation analysis was conducted between the changes of RT (ΔRT, in percentage) and relative EEG (P_δ, ΔP_δ, P_θ, ΔP_θ) to investigate the behavior–EEG relationship in the immediate effects and general effects in different sessions.

Normality and sphericity of data were checked for statistical analysis. A value of $p < 0.05$ was considered significant. All statistical processes were performed using the SPSS 25.0 software package (SPSS, Chicago, IL).

Results

Behavioral results

To investigate the time-on-task (TOT) effect induced by PVT, we averaged the reaction time (RT) in the *No-Break* session into 10 3-min bins to evaluate the trend of behavioral performance over the task (Figure 3A, gray curve). As expected, performing PVT led to a significant TOT effect, manifesting increments in RT similar to our previous studies (Sun et al., 2017). Specifically, a significant increase [$F_{(3,54)} = 22.270$, $p < 0.001$, $\eta^2 = 0.553$] of reaction time was observed from T1 to T4. The individually fitted linear slope of the RT also showed a performance decline throughout the task (slope Mean $\pm$ SD = 0.022 ± 0.004), in which averaged RT was 11.78% longer during T4 (most fatigued) in comparison with T1 (most vigilant).

For the immediate effect (T2 vs. T3) of mid-task breaks (Figure 3B), there were significant main effects for time-by-session interaction [$F_{(2,36)} = 4.942$, $p = 0.013$, $\eta^2 = 0.215$], time [$F_{(1,18)} = 25.713$, $p < 0.001$, $\eta^2 = 0.588$], and session [$F_{(2,36)} = 7.421$, $p = 0.002$, $\eta^2 = 0.292$]. Following *post-hoc* analyses indicated that the significant interaction effect was attributed to the decrease of RT in both the *Exercise-Break* session [$F(1, 18) = 16.448$, $p = 0.001$, $\eta^2 = 0.477$] and the *Rest-Break* session [$F_{(1,18)} = 17.838$, $p = 0.001$, $\eta^2 = 0.498$]. However, no significant difference was observed between the *Exercise-Break* session and *Rest-Break* session in their post-break RT, indicating a similar vigilance improvement immediately after different interventions.

The general effect (T1 vs. T4) of mid-task breaks was also tested (Figure 3C). Significant main effects were found for time [$F_{(1,18)} = 65.451$, $p < 0.001$, $\eta^2 = 0.784$] and sessions [$F_{(2,36)} = 4.655$, $p = 0.016$, $\eta^2 = 0.205$], but no time-by-session interaction [$F_{(2,36)} = 2.059$, $p = 0.142$, $\eta^2 =$

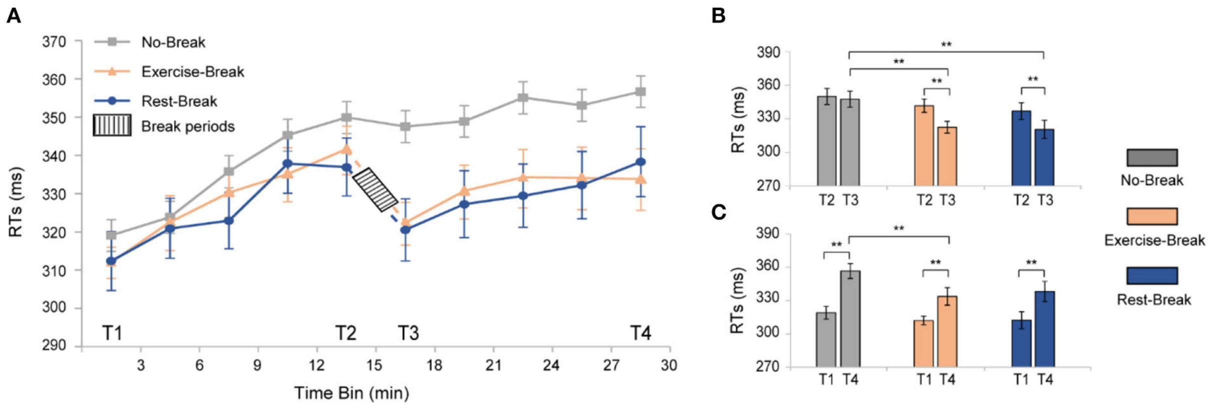


FIGURE 3
Behavioral results for the three different sessions. **(A)** RTs of PVT task segmented into 3-min bin. **(B)** *post-hoc* analyses for the immediate effect of mid-task interventions. **(C)** *Post-hoc* analyses for the general effect of the mid-task breaks. $^{**}p < 0.01$. Error bars represent the mean ± SEM.

0.103]. Follow-up *post-hoc* comparisons for the main time effect suggested that RT in T4 was significantly longer than that in T1 ($p < 0.001$ in all sessions). Specifically, compared with T1, RTs in *Exercise-Break* and *Rest-Break* sessions increased by 6.970 and 8.297%, respectively. In addition, *post-hoc* comparisons for the main session effect indicated that in the T4, the RT in the *Exercise-Break* session was significantly shorter than that in the *No-Break* session [$F_{(1,18)} = 8.431$, $p = 0.009$, $\eta^2 = 0.319$].

In terms of subjective states, significant main effect of time was found on both engagement [$F_{(1,18)} = 21.535$, $p < 0.001$, $\eta^2 = 0.545$] and distress [$F_{(1,18)} = 8.568$, $p = 0.009$, $\eta^2 = 0.322$] scores, but no significant difference of session [engagement: $F_{(2,36)} = 1.032$, $p = 0.367$, $\eta^2 = 0.054$; distress: $F_{(2,36)} = 1.762$, $p = 0.186$, $\eta^2 = 0.089$] and time-by-session [engagement: $F_{(2,36)} = 0.804$, $p = 0.455$, $\eta^2 = 0.043$; distress: $F_{(2,36)} = 0.113$, $p = 0.894$, $\eta^2 = 0.006$] interaction. Further inspection of the main effect in time suggested that for *No-Break* and *Exercise-Break* session, participants showed significantly increased distress [*No-Break* session: $F_{(1,18)} = 13.986$, $p = 0.001$, $\eta^2 = 0.437$; *Exercise-Break* session: $F_{(1,18)} = 6.495$, $p = 0.02$, $\eta^2 = 0.265$] as well as less engagement [*No-Break* session: $F_{(1,18)} = 17.618$, $p = 0.001$, $\eta^2 = 0.495$; *Exercise-Break* session: $F_{(1,18)} = 4.015$, $p = 0.06$, $\eta^2 = 0.182$] in the post-session compared with pre-session, indicating a similar trend of subjective experience between successive PVT and exercise-inserted PVT.

EEG power changes in immediate effect

The immediate effect of mid-task breaks on the EEG power ratio was first assessed. We observed a significant difference in theta and delta activities in T3 (post-break bin) compared with T2 (pre-break bin). Specifically, in theta band, there were significant main effects for time-by-session interaction, in $P_{\theta\_Frontal}$ [$F_{(2,36)} = 5.848$, $p = 0.006^*$, $\eta^2 = 0.245$; * indicated survive FDR threshold at $q < 0.05$ for interaction effect analysis] and $P_{\theta\_Parietal}$ [$F_{(2,36)} = 3.886$, $p = 0.030^*$, $\eta^2 = 0.178$]. Following *post-hoc* analysis indicated that, in the *Exercise-Break* session, P_θ significantly decreased in T3 compared with T2, in $P_{\theta\_Frontal}$ [$F_{(1,18)} = 11.528$, $p = 0.003$, $\eta^2 = 0.390$], $P_{\theta\_Parietal}$ [$F_{(1,18)} = 21.381$, $p < 0.001$, $\eta^2 = 0.543$] in comparison with a maintained P_θ in *Rest-Break* and *No-Break* sessions (Figure 4).

And in delta band, there were significant main effects for time-by-session interaction, in $P_{\delta\_Central}$ [$F_{(2,36)} = 3.443$, $p = 0.043$, $\eta^2 = 0.161$]. The *post-hoc* analysis indicated that, in the *Exercise-Break* session, $P_{\delta\_Central}$ significantly increased in T3 compared with T2 [$F_{(1,18)} = 4.676$, $p = 0.044$, $\eta^2 = 0.206$] (Figure 5).

EEG power changes in general effect

We assessed the general effect of mid-task breaks by comparing the EEG power ratio in T4 (last 3-min bin of the whole session) with T1 (first 3-min bin). A significant main effect for time-by-session interaction was also observed in $P_{\delta\_Central}$ [$F_{(2,36)} = 5.221$, $p = 0.010^*$, $\eta^2 = 0.225$]. The *post-hoc* comparison showed a significant decrease in T4 compared to T1 [$F_{(1,18)} = 6.171$, $p = 0.023$, $\eta^2 = 0.255$] in the *Rest-Break* session, as well as an increase trend [$F_{(1,18)} = 3.212$, $p = 0.090$, $\eta^2 = 0.151$] in the *Exercise-Break* session (Figure 6).

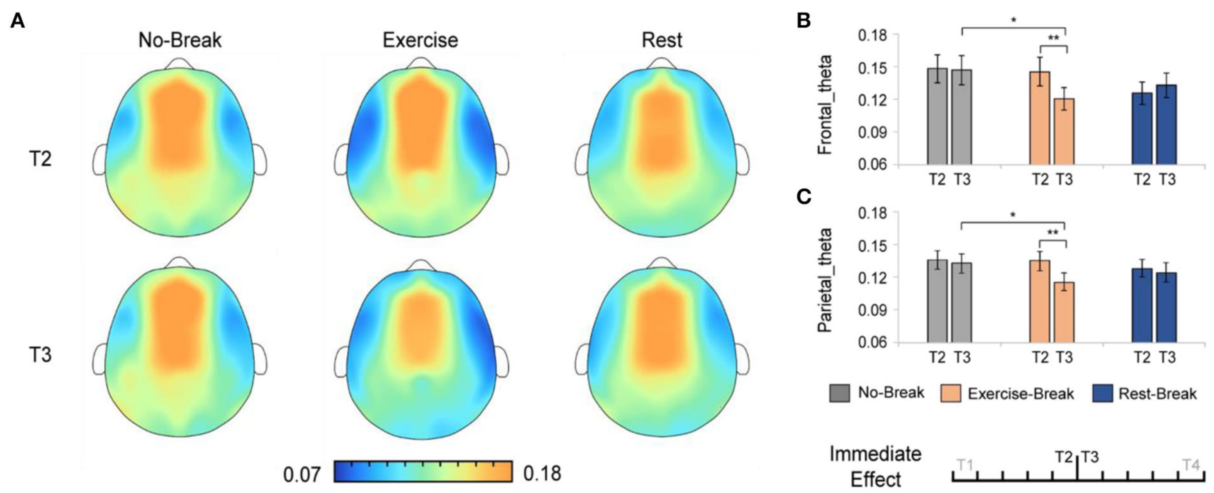


FIGURE 4
The theta spectral changes in immediate effect (T2 *vs.* T3). **(A)** The brain topography of the immediate effect of the mid-task breaks on theta activities. The EEG power ratios of the **(B)** frontal and **(C)** parietal theta in the pre-break bin (T2) and post-break bin (T3). $^{**}p < 0.01$; $^{*}p < 0.05$. Error bars represent the mean ± SEM.

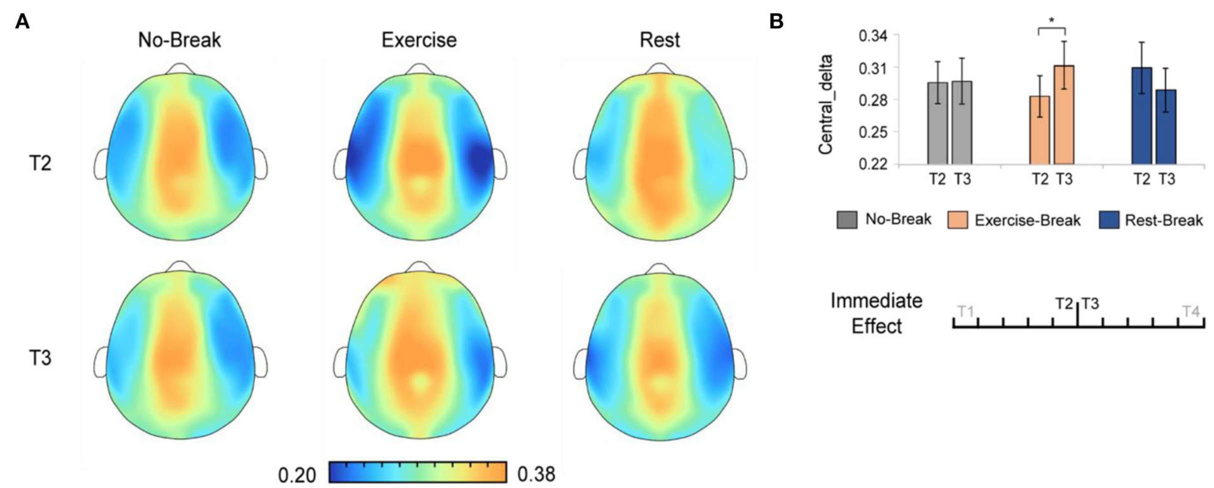


FIGURE 5
The delta spectral changes in immediate effect (T2 *vs.* T3). **(A)** The brain topography of the immediate effect of the mid-task breaks on delta activities. **(B)** The EEG power ratios of the central delta in the pre-break bin (T2) and the post-break bin (T3). $^{*}p < 0.05$. Error bars represent the mean ± SEM.

Correlation in EEG power and reaction time changes

According to the analysis of immediate and general effect, P_δ and P_θ demonstrated significant differences immediately after the *mid-task exercise*, while P_δ also suggested a significant difference in the general effect of the *Rest-Break* session. Consistent with the interaction effect observed in EEG power, correlation analyses were mainly focused on the immediate effect of the *Exercise-Break* session and the general effect of the *Rest-Break* session. Correlation investigation between the EEG power and behavioral performance showed that P_θ in T2 was correlated with ΔRT_{T3-T2} ($r_{19} = -0.502$, $p = 0.028$) in the exercise-inserted task, and P_δ in T3 ($r_{19} = 0.537$, $p = 0.018$) was significantly related with ΔRT_{T4-T1} in the rest-intervention task. No significant association was observed between $\Delta P_{\theta T3-T2}$ and ΔRT_{T3-T2} ($r_{19} = 0.124$, $p = 0.613$), $\Delta P_{\delta T3-T2}$ and ΔRT_{T3-T2} ($r_{19} = -0.055$, $p = 0.822$) in *Exercise-Break* session, as well as $\Delta P_{\delta T4-T1}$ and ΔRT_{T4-T1} ($r_{19} = -0.425$, $p = 0.070$) in *Rest-Break* session. In particular, the

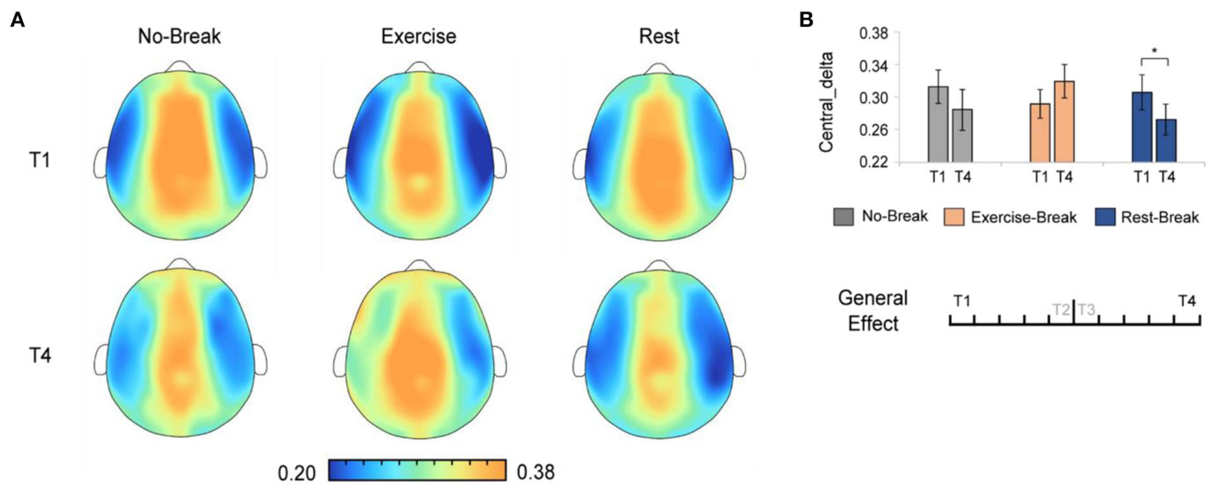


FIGURE 6
The delta spectral changes in general effect (T1 *vs.* T4). **(A)** The brain topography of the general effect of the mid-task breaks on delta activities. **(B)** The EEG power ratios of the central delta in the session-start bin (T1) and session-end bin (T4). $^*p < 0.05$. Error bars represent the mean ± SEM.

EEG power in correlation analysis was acquired from global electrodes rather than specific clusters to preliminarily explore the biomarker of mental fatigue recovery (Figure 7).

Discussion

In this study, we revealed divergent post-break improvement neural patterns following mid-task exercise and rest break under similar beneficial effects on behavioral performance, and further investigated the neural basis underlying mental fatigue restoration. The significant findings are as follows: (1) behaviorally, we found a transiently restorative effect of both exercise and rest breaks on sustained attention, without any general beneficial effect on behavioral performance. (2) Exercise and rest demonstrated different patterns of EEG change in post-break improvement. In particular, theta decreased and delta increased immediately after the *mid-task exercise*, while decreased delta was induced near the end of the *Rest-Break* session. (3) Correlation analysis suggested that the immediate improvement of behavioral performance (i.e., ΔRT_{T3-T2}) for exercise intervention was associated with theta power in T2. Interestingly, we found the general behavioral effect (i.e., ΔRT_{T4-T1}) in the *Rest-Break* session was correlated with delta power in T3. These findings are discussed in greater detail below.

Behavioral effects of the mid-task breaks

Both the mid-task exercise and rest induced similar immediate improvements as shown in the significantly reduced RT in the post-break window. For the *mid-task rest*, this behavioral result was inconsistent with our early findings that no significant restorative effect was observed after rest breaks (Sun et al., 2017). This discrepancy could stem from the different duration of the rest admitted to the participants, i.e., 5 min in Sun et al. (2017) *vs.* 15 min in the current work. Embracing previous observations with the current findings, we could therefore infer that a longer rest break might be needed to induce substantial recovery from mental fatigue (Ross et al., 2014; Helton and Russell, 2015). Further evidence to support this notion was from a behavioral study quantitatively investigating the effect of rest in three different durations for TOT recovery, which demonstrated that longer rest break produced a better restoration (Lim and Kwok, 2015). However, no significant recovery was observed at the end of the *Rest-Break* session in our results. This is in line with the previous study that TOT decrements tended to be steeper after long than short breaks (Lim and Kwok, 2015). As a result, providing participants with a *mid-task rest* with the time duration of 15 min might only produce a transient restoration restricted to the period right after the midway break.

The *mid-task exercise* breaks were found to be capable of replenishing the behavioral performance immediately, fairly as much as rest did. Notably, these results were consistent with accumulating evidence that aerobic exercise produced a more robust positive effect on cognitive and attention (Pontifex et al., 2019). This was also partly consistent with the arousal theory, which indicated that exercise-induced brain activation, especially in the prefrontal cortex (Popovich and Staines, 2015), the region critical for sustained attention. Our work extends the above findings by linking the positive

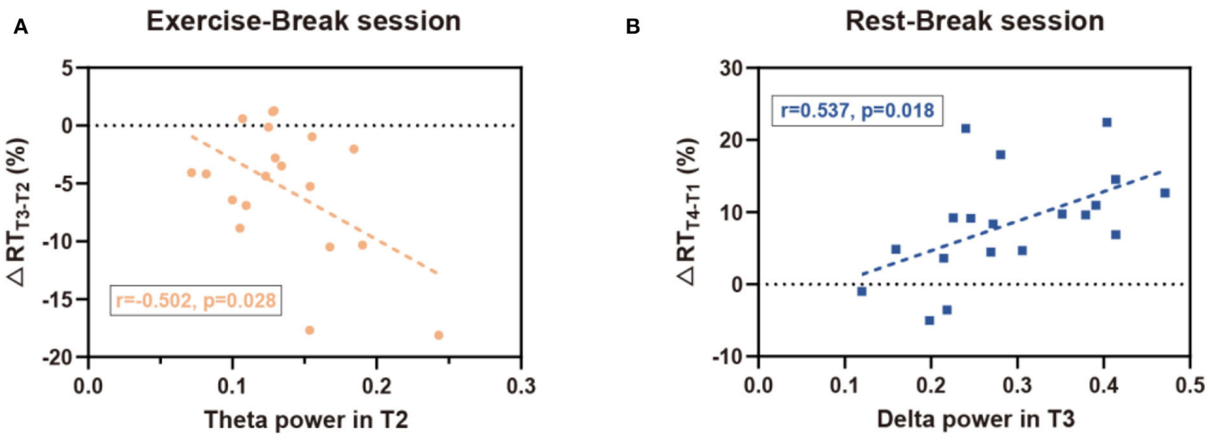


FIGURE 7
Correlation results for EEG-behavior analysis. **(A)** In the Exercise-Break session, RT change (in percentage) from T2 to T3 was negatively correlated with EEG theta power in T2. **(B)** In the Rest-Break session, RT change (in percentage) from T1 to T4 was positively correlated with EEG delta power in T3.

effects of exercise to the practical application of mental fatigue restoration.

More interestingly, we found the subjective distress score in SSSQ, a measure of negative affect, kept consistent in the *Rest-Break session*, while increased in the *No-Break* session and *Exercise-Break session*. This indicated that after the 15-min cycling break, subjects might not feel recovered from mental fatigue, even though there were indeed apparent improvements in their vigilance. In addition, the trend of engagement scores in SSSQ also reflected a similar phenomenon. Put differently, although both rest and exercise could intervene TOT effect immediately, subjects might have different recognition of their "feeling about mental fatigue," which might correspond to divergent cognitive processes underlying the similar behavioral performance improvement.

Neural patterns following exercise-induced attention improvement

As for the *mid-task exercise*, a significant reduction of theta activity in the frontal and parietal cortex areas was observed in the immediate post-break period. Frontal theta has been repeatedly reported as a reliable index for mental fatigue (Lal and Craig, 2001; Wascher et al., 2014), and an increase in frontal theta may reflect exhausting cognitive control resources with increasing TOT (Clayton et al., 2015). For example, studies found that reduced frontal theta was associated with better performance in action execution, while higher frontal theta might reflect an excessive consumption of attention engagement and hamper the task performance (Kao et al., 2013). Besides, a significant theta power increase in the frontal was believed to reflect a more demanding attention control process that originated in the anterior cingulate cortex (ACC) (Sauseng et al., 2010). This ACC-mediated theta activity has been believed to be associated with externally oriented monitoring and executive control (Cavanagh and Frank, 2014; Cohen, 2017). From the correlation analysis, we further observed that a greater before-intervention P_θ was associated with more behavioral restoration after *mid-task exercise* in our study. In summary, the reductions in theta following exercise break might reflect optimized monitoring and allocation of executive control resources toward external goals so as to ameliorate TOT declines. In other words, the *mid-task exercise* matched the current attention to the desired level.

Besides, a significant increase in the central delta was also observed right after exercise intervention. Consistent with our results, the delta increase has been repeatedly reported immediately after exercise (Mechau et al., 1998; Crabbe and Dishman, 2004). The traditional view toward the increase of delta recognized it as the biomarker of fatigue. For instance, in laboratory-controlled driving simulating studies, increases in delta activity were found during the transition into the fatigued state (Lal and Craig, 2002). Unlike these findings, an increased delta ratio was observed in the current work where significant improvements in behavioral performance were revealed after cycling exercise, which might suggest a beneficial effect of the increased post-exercise delta. Of note, in addition to fatigue-related alterations, the increased delta power has also been reported to be associated with inhibition of the internal interferences that might affect the task performance (Harmony, 2013), which may lead to the observed increased post-exercise delta power. For example, during a Go/No-Go task in 15 normal young volunteers, delta activity increases were clearly demonstrated while subjects inhibited their movement (Harmony et al., 2009). Besides, another research suggested that there was a reciprocal relationship between alpha and delta activity, which reflected the inhibitory control over motivational and emotional drives (Knyazev, 2007). In summary, we inferred that the delta increases after exercise suggested an inhibitory effort toward possible interference thoughts, which in turn improved the performance and represented fatigue recovery.

In sum, these findings could fit some of the predictions in the oscillatory frequencies model of sustained attention (Clayton et al., 2015), in which attention is adjusted through the excitation of task-relevant cognitive processes and the inhibition of task-irrelevant cognitive processes. The decrease of theta after exercise could demonstrate a more effective cognitive monitoring and manipulation in primary sustained attention tasks. And the increase of delta might reflect the need for inhibiting task-irrelevant thoughts during a primary mental task. The two approaches together could promote the performance of post-break behavioral performance.

The neural strategy of mid-task rest for handling TOT effect

In contrast with the post-exercise effect, EEG change was not observed immediately after rest intervention in low-frequency power spectral but manifested as a drop in delta power at the end of the task when the TOT effect reappeared. In addition to the biomarker of mental fatigue and internal inhibition, delta power was also considered associated with negative effects (Wu et al., 2019; Zheng et al., 2019) and subjective sleepiness (Phipps-Nelson et al., 2011). Therefore, the decrease of the delta at the end of the *Rest-Break Session* could be illustrated as the active emotion and motivation toward sustained attention task, so that participants would respond positively when mental fatigue was induced once again. This beneficial effect brought by *mid-task rest* could also be validated from the subjective feeling feedback, in which subjects maintained the effect and motivation from the start to the end of the *Rest-Break Session*, while both the *No-Break Session* and *Exercise-Break Session* suggested increased subjective distress and declined task engagement. In addition, we found that the level of delta power following rest was associated with long-term behavioral performance based on correlation analysis. In detail, a lower delta power after rest corresponded to a higher sustained attention level before the end of the task, and the delta could be used as a neurological indicator demonstrating the vigilance level after rest. In sum, *mid-task rest* improved the subjective experience to counter TOT effects, which could be manifested in the delta power after rest intervention.

Future consideration

Some issues should be considered when interpreting our results. First, a within-subject design was adopted in this study to neutralize the widely revealed between-subject variability toward the TOT effect (Parasuraman and Jiang, 2012). Although this is an advantage of the study design, our sample size was subsequently small, and only healthy and young participants were recruited given the amounts of labor in repeated measure (i.e., each participant should come to the lab once a week for continuous 3 weeks without dropout). Therefore, more experimental studies are needed to further validate our findings with a broad age range and a larger independent sample. Besides, subjects were instructed to keep their eyes open with gaze at a central fixation cross during the mid-task rest. It is a more practical way of performing the experiment without the need to give a cue to tell subjects to open their eyes or if concern of falling asleep during the experiment that might induce additional confounding factors compared to a natural eye-closed rest. In fact, a study of multi-center neuroimaging data showed that data collection with eyes closed showed more sleep than the fixation group, suggesting that fixation supports the maintenance of wakefulness (Tagliazucchi and Laufs, 2014). Nonetheless, in a real-life situation, people intend to take a break in an ecologically valid way, with an unconstrained activity that is more relaxing. Therefore, future studies could pay more attention to the naturality and validity of the mid-task breaks to explore the practical restoration approach for a particular application scenario. Second, to induce significant performance decrement, the simple and monotonous PVT task was introduced in this study, which was considered to be more stressful and effortful than complex tasks (Langner and Eickhoff, 2013). In fact, handling multiple tasks were common and important in daily life, with a series of decision-making, alertness, or physical movement, corresponding to more sophisticated activating states of the brain. Therefore, future work could consider the paradigm design consisting of simulated real-world working assignments to further verify the effectiveness of the divergent fatigue-intervention strategy. Third, based on the cortical oscillation model (Clayton et al., 2015), we found that the excitation of task-relevant cognitive processes and the inhibition of task-irrelevant processes could explain the EEG change in theta and delta following *mid-task exercise*. It is noteworthy mentioning that we did not directly distinguish the task-irrelevant cognitive state from the performance of external stimuli response in the current work. As a result, future research may especially focus on the brain status after break intervention through the neurofeedback technique to further investigate our novel interpretation.

Conclusion

In summary, this study provided one of the first looks into the neural mechanism of recovery strategy recruited by different breaks, through evaluating the behavioral performance and spatio-spectral characteristics of low-band EEG following rest and exercise break in a sustained attention task. Our findings provided behavioral and electrophysiological evidence to demonstrate that divergent neural patterns were recruited by mid-task rest and exercise though vigilance restoration was similar, indicating different neural strategies to counter TOT effects. Our work broadens the knowledge of mental fatigue countermeasure and may lead to further mechanism study in neuroscience and psychology, as well as real-world ergonomics for various TOT restoration situations.

Data availability statement

The raw data supporting the conclusion of this article is available upon reasonable request to the corresponding authors.

Ethics statement

The studies involving human participants were reviewed and approved by Zhejiang University. The patients/participants provided their written informed consent to participate in this study.

Author contributions

Conceptualization, resources, and funding acquisition: PQ and YS. Methodology: SW, LZ, LG, JY, GL, PQ, and YS. Formal analysis: SW and LZ. Writing—original draft preparation: SW, LZ, and YS. Supervision: YS. All authors have read and agreed to the published version of the manuscript.

Funding

This work was funded by the National Natural Science Foundation of China (Grant Nos. 82172056, 51905379, and 81801785), the National Key Research and Development Program of China (Grant No. 2021ZD0200400), the Key Research and Development Program of Zhejiang Province (Grant No. 2022C03064), the Zhejiang University Global Partnership Fund (Grant No. 100000-11320), and the Hundred-Talent Program of Zhejiang University. This work was partially supported by the Shanghai Municipal Science and Technology Major Project (Grant No. 2021SHZDZX0100) and the Fundamental Research Funds for the Central Universities.

Acknowledgments

We acknowledge the assistance of Miss. Yuqin Han and Mr. Qia Hu for data collection.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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frontiers | Frontiers in Human Neuroscience

TYPE Original Research
PUBLISHED 03 October 2022
DOI 10.3389/fnhum.2022.950893

OPEN ACCESS

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SPECIALTY SECTION
This article was submitted to
Cognitive Neuroscience,
a section of the journal
Frontiers in Human Neuroscience

RECEIVED 23 May 2022
ACCEPTED 13 September 2022
PUBLISHED 03 October 2022

CITATION
Shi D, Geng F, Hao X, Huang K and Hu Y (2022) Relations between physical activity and hippocampal functional connectivity: Modulating role of mind wandering.
Front. Hum. Neurosci. 16:950893.
doi: 10.3389/fnhum.2022.950893

Relations between physical activity and hippocampal functional connectivity: Modulating role of mind wandering

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Physical activity is critical for maintaining cognitive and brain health. Previous studies have indicated that the effect of physical activity on cognitive and brain function varies between individuals. The present study aimed to examine whether mind wandering modulated the relations between physical activity and resting-state hippocampal functional connectivity. A total of 99 healthy adults participated in neuroimaging data collection as well as reported their physical activity in the past week and their propensity to mind wandering during typical activities. The results indicated that mind wandering was negatively related to the resting-state functional connectivity between hippocampus and right inferior occipital gyrus. Additionally, for participants with higher level of mind wandering, physical activity was negatively related to hippocampal connectivity at left precuneus and right precentral gyrus. In contrast, such relations were positive at right medial frontal gyrus and bilateral precentral gyrus for participants with lower level of mind wandering. Altogether, these findings indicated that the relations between physical activity and hippocampal functional connectivity vary as a function of mind wandering level, suggesting that individual differences are important to consider when we aim to maintain or improve cognitive and brain health through increasing physical activity.

KEYWORDS

physical activity, mind wandering, hippocampus, resting-state functional connectivity, cognitive function

Introduction

There is no doubt that physical activity is critical for maintaining cognitive and brain health throughout the lifespan (Hillman et al., 2008; Duzel et al., 2016). Physical activity is also known as a "medicine" due to its protective effects against cognitive declines (American College of Sports Medicine, 2009). Many studies have found that increased physical activity is associated with better cognitive performance, such as attention, visuospatial processing, cognitive control, and memory (Colcombe and Kramer, 2003; Donnelly et al., 2016; de Greeff et al., 2018). However, the neural mechanisms underlying the effect of physical activity on cognitive functions are still not clear. To address the issue, many neuroimaging studies have focused on the changes in neural structure and function associated with physical activity (Colcombe et al., 2004, 2006; Pontifex et al., 2011; Chen et al., 2019; Horowitz et al., 2020). Of all the documented brain structure and functional changes that responds to physical activity, robust changes have been observed in the hippocampus (Clark et al., 2012; Prakash et al., 2015; Rendeiro and Rhodes, 2018).

Hippocampus plays a critical role in integrating information during learning, memory consolidation, and retrieval (Tulving and Markowitsch, 1998; Lavenex and Lavenex, 2013). It has been shown in rodent models that increases in physical activity are associated with increased hippocampal neurogenesis (van Praag et al., 2005) and enhanced hippocampal long-term potentiation (van Praag et al., 1999; Liu et al., 2011). Moreover, physical activity has been found to modify the hippocampus at the molecular and morphological level (van Praag et al., 1999; Stranahan et al., 2007; Liu et al., 2011), and these modifications are thought to contribute to the improvements in hippocampal-dependent memory, learning, and other cognitive functions (Rendeiro and Rhodes, 2018).

Similarly, researchers also sought to understand the influence of physical activity on the hippocampus in humans (Erickson et al., 2009, 2011; Ruscheweyh et al., 2011; Chaddock et al., 2016). For instance, randomized controlled clinical trials indicated that people with higher physical activity or better fitness showed greater hippocampal volume (Chaddock et al., 2010, 2016). Such exercise-related changes in hippocampal volume were related to subsequent changes in memory performance (Erickson et al., 2009, 2011; Maass et al., 2015). The profound effect of physical activity on hippocampal structure has led researchers to explore how physical activity may impact hippocampal function, as measured by brain activation (Pereira et al., 2007; Burdette et al., 2010; Voelcker-Rehage et al., 2011), and functional connectivity between the hippocampus and other brain regions (Burdette et al., 2010; Chaddock et al., 2010; Voss et al., 2010; Prakash et al., 2011; Ikuta et al., 2019). For example, level of vigorous physical activity was significantly associated with right hippocampal-orbitofrontal connectivity during resting state (Ikuta et al., 2019). Furthermore, an intervention study indicated that 12-month physical exercise training in old adults increased the negative connection between prefrontal regions and anterior left hippocampus region during resting state (Voss et al., 2010). Another study found that the group who received 4-month aerobic exercise training showed greater connectivity between hippocampus and anterior cingulate cortex than the control group (Burdette et al., 2010).

However, whether individuals can get cognitive benefits from physical activity and how much benefit they can get vary from person to person (Madden et al., 1989; Rhodes and Smith, 2006; Fedewa and Ahn, 2011). The routes by which physical activity affects learning and memory are complex and may likely be moderated by many factors, including age, gender, health status, cognitive level, and numerous psychosocial factors (Tomporowski et al., 2011). For example, a meta-analysis study showed that children of different ages may get various degrees of cognitive benefits from physical activity, indicating that age may be an important moderator of the benefits of physical activity (Benjamin and Jennifer, 2003). Moreover, the relations of physical activity to cognitive functions and hippocampal volume differ by gender, with females obviously benefiting from physical activity to a greater extent than males (Barha et al., 2020). Therefore, before physical activity can be prescribed as "medicine" for the brain, it is important to better understand the factors contributing to this variation.

Mind wandering, as an important cognitive function supported by hippocampus (Faber and Mills, 2018; Mills et al., 2018), may moderate the relations of physical activity to learning and memory. Mind wandering is defined as thoughts that were not tied to concurrent perceptions, which occurs when the attention shifts away from the present situation to one's inner thought (Singer, 1966; Smallwood et al., 2003). The resting-state functional connectivity within default mode network (DMN), within which the hippocampus is a node, has been shown to be closely related to self-generated thoughts that involved in mind wandering (Christoff et al., 2009; Andrews-Hanna, 2011; Xu et al., 2014; Ellamil et al., 2016; Mittner et al., 2016). For example, hippocampus was more activated during mind wandering than at rest, suggesting that mind wandering may induce the activation of hippocampus (Xu et al., 2014).

Furthermore, previous studies also suggested that mind wandering was related to future physical activity (Smallwood and Andrews-Hanna, 2013; Fanning et al., 2016). For instance, present-moment mind wandering was positively associated with future moderate-to-vigorous physical activity, indicating that the nature of one's mind wandering may impact the ability to plan for or engage in the goal directed behavior (Fanning et al., 2016). Although few studies have directly tested the relations between physical activity and mind wandering, previous studies have repeatedly found that increasing physical activity improves sustained attention (Kumar et al., 2015; Luque-Casado et al., 2015; Ciria et al., 2017). For example, an ERP study found that higher aerobic fitness was related to neuroelectric activity, demonstrating a better overall sustained attention and the ability to allocate attentional resources (Luque-Casado et al., 2015). Therefore, mind wandering, as a cognitive activity supported by hippocampus, is also closely related to physical activity.

To sum, previous studies have shown that physical activity, mind wandering and hippocampal functions are related to each other (Voelcker-Rehage et al., 2011; Smallwood and Andrews-Hanna, 2013; Faber and Mills, 2018). Specifically, physical activity not only has positive impact on hippocampal functions, but also affects mind wandering (Luque-Casado et al., 2015; Chaddock et al., 2016). Additionally, mind wandering also affects hippocampal activity due to its role in inducing hippocampal activation (Xu et al., 2014; Ellamil et al., 2016). However, it is still unknown that whether mind wandering plays a role in the effect of physical activity on hippocampal functions. To provide insight into this question, the purpose of this study is to test whether mind wandering modulated the relations between physical activity and hippocampal functional connectivity measured during resting state. Specifically, we hypothesized that the relations between physical activity and hippocampal functional connectivity vary as a function of individual's mind wandering level.

Materials and methods

Participants

A total of 105 college students were recruited from Zhejiang University at Hangzhou in China (mean age = 22.78, SD = 2.91, 49 female). Six participants were excluded from final analyses due to excessive head motion during fMRI scanning ($n = 1$) or incomplete questionnaires ($n = 5$). All participants were healthy without adverse health conditions, physical disabilities, or neurological disorders. This study was approved by the research ethics review board of Zhejiang University. Participants signed consent forms before participating in the study.

Questionnaires

International physical activity questionnaire

Participants completed the short version of International Physical Activity Questionnaire (IPAQ) to measure their physical activity level during the last 7 days (Hagströmer et al., 2006). The items in the questionnaire were structured to measure the volume of vigorous-intensity activity, moderate-intensity activity, and walking per week. These activities were weighted by their energy requirements defined in MET (Metabolic Equivalent Task) to generate a score in MET-minutes, which is calculated by multiplying the MET score of an activity by the minutes performed. Total physical activity (MET-min/week) was calculated by the summation of vigorous, moderate activity, and walking in MET-minutes over a week. This summation score was used as a continuous variable to measure the physical activity level of participants in the current study.

Mind wandering questionnaires

The Mind Wandering Questionnaire (MWQ) (Mrazek et al., 2013) is a 5-item self-report scale, which was used to measure the propensity to mind wandering during typical activities (Cronbach's $\alpha = 0.85$). We used the Chinese version of the MWQ, which was verified to be a suitable tool to measure the trait level of mind-wandering (Luo et al., 2016). The questionnaire is a 6-point Likert scale, ranging from 1 (Never) to 6 (Always), with participants rating these items based on how often they experienced the particular situation (e.g., "I find myself listening with one ear, thinking about something else at the same time" or "I mind-wander during lectures or presentations"). Higher scores represent greater propensity to mind wandering.

Imaging data acquisition and preprocessing

Participants were scanned in a Siemens 3.0T scanner (MAGNETOM Prisma, Siemens Healthcare, Erlangen, Germany) with a 20-channel coil in the Brain Imaging Science and Technology Center at Huajiachi Campus of Zhejiang University. They were asked to maintain their gaze at the fixation square in the center of the screen while they could blink as usual. Additionally, we explained to participants how subtle movements could affect data quality and asked them to remain as still as a statue to minimize head movement. The high-resolution structural images were acquired using a T1-weighted magnetization prepared-rapid gradient-echo sequence with the following parameters: TR = 2300 ms, TE = 2.32 ms, slice thickness = 0.9 mm, voxel size = $0.90 \times 0.90 \times 0.90$ mm^3, voxel matrix = 256×256, flip angle = 8°, and field of view = 240 mm^2, duration of 7 min and 26 s. Then, a total of 480 whole-brain resting-state volumes were collected using a T2-weighted gradient echo planar imaging sequence: TR = 1000 ms, TE = 34 ms, slice thickness = 2.5 mm, voxel size = $2.50 \times 2.50 \times 2.50$ mm^3, voxel matrix = 92×92, flip angle = 50°, field of view = 230 mm^2, slices = 52, and duration of 8 min.

The following steps were carried out to preprocess the data: (1) Slice timing correction and head motion correction were performed using AFNI.[1] (2) Tissue segmentation was conducted to extract brains using SPM12.[2] ANTs[3] was used to co-register

1 https://afni.nimh.nih.gov/
2 https://www.fil.ion.ucl.ac.uk/spm/
3 http://stnava.github.io/ANTs/

and normalize structural and functional images from original space to MNI space. (3) All functional images were spatially smoothed using a 5 mm full-width-at-half-maximum Gaussian kernel. (4) Nuisance variable regression was conducted using six-rigid head motion and their forward derivate as well as the first five principal components from white matter and cerebral spinal fluid (CSF) separately. (5) A band-pass filtering (0.01–0.1 Hz) was applied.

Since the resting-state functional connectivity could be influenced by small volume-to-volume head movements, we first calculated the framewise displacement (FD) of each volume to quantify the head motion. Any volume with FD $\geq$ 0.5 mm as well as 1 back and 1 forward volumes were scrubbed to minimize the effect of head motion. The mean FD of all participants included in the final statistical analyses was from 0.09 to 0.30 (mean FD = 0.153, SD = 0.038) with data length $\geq$ 7 min.

Then we performed resting-state functional connectivity analyses by using AFNI. We obtained the hippocampal seed regions from the Harvard–Oxford subcortical structure probabilistic atlas[4] thresholded at 25%. With the uncal apex served as the border between anterior and posterior hippocampus (Duvernoy, 2005), the hippocampus was divided into anterior and posterior segments using manual identification of standard anatomical landmarks by using 1-mm MNI152 template.[5] Therefore, left anterior, right anterior, left posterior, and right posterior hippocampus were used as seed regions. The functional connectivity between the time series of the seed regions and the other regions throughout the whole brain was calculated to generate the individual resting-state functional connectivity map (*r*-map). Then, by using Fisher's r-to-z transformation, the *r*-maps were converted into z-maps to obtain the normally distributed values of the connectivity maps.

Statistical analysis

Statistical analyses were conducted using 3dLME program within AFNI. To identify whether there were interactions between physical activity and mind wandering in predicting the functional connectivity between hippocampus and other brain regions, we added physical activity, mind wandering, and their interaction as independent variables in the fixed effect model. Since previous studies have found functional separation of hippocampus in different subregions and hemispheres (Strange et al., 1999; Iglói et al., 2010; Shipton et al., 2014; Robinson et al., 2015; Persson et al., 2018), we included the Subregions (anterior vs. posterior) and Hemispheres (left vs. right) as within-subject covariables. Random effects were also added to the model. The 3dClustSim in AFNI indicated that when $p_{uncorrected}$ < 0.001, only clusters with a minimum of 23 voxel size were viewed as significant with multiple comparison correction ($p_{uncorrected}$ < 0.001). We mainly reported the results involving physical activity, mind wandering, or both.

4 https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/Atlases

5 http://www.bic.mni.mcgill.ca/ServicesAtlases/ICBM152NLin2009

Results

Relation between physical activity and mind wandering

Table 1 showed the characteristics of participants who contributed both fMRI and questionnaires data. There was no significant correlation between physical activity and mind wandering (p = 0.094). Additionally, both of them were not significant related to mean FD (r = −0.048, p = 0.637; r = −0.004, p = 0.966). Therefore, mean FD was not included as covariate when we tested brain-behavioral relations below.

Relation of physical activity and mind wandering to hippocampal functional connectivity

There was a significant main effect of mind wandering at right inferior occipital gyrus (Cluster size = 30; x = 45, y = −65, z = −14), suggesting that mind wandering was negatively related to the resting-state functional connectivity between hippocampus and right inferior occipital gyrus (Figure 1). Physical activity was not significantly related to hippocampal functional connectivity at any brain region. However, there were interactions between physical activity and mind wandering in predicting hippocampal functional connectivity at left precuneus, precentral gyrus, left superior frontal gyrus, and right medial frontal gyrus (Table 2).

To understand these interactions, we separated all participants into high (48 subjects, 22 females, mean age = 22.71, SD = 2.75) and low groups (51 subjects, 27 females, mean age = 22.75, SD = 3.05) according to the mean scores of their mind wandering (i.e., 16.73). Then, for each group, we conducted whole-brain search analyses to test whether physical activity was related to hippocampal functional connectivity at each brain region showing significant interaction. The results indicated that in high mind wandering group, physical activity was negatively related to hippocampal functional connectivity at left precuneus and right precentral gyrus (Figure 2). In contrast, in low mind wandering group, there were positive correlations between physical activity and hippocampal functional connectivity at right medial frontal gyrus, right precentral gyrus, and left precentral gyrus (Figure 3 and Table 3). However, the relations between physical activity and hippocampal functional connectivity at left superior frontal

TABLE 1 Characteristics for participants who contributed both fMRI and questionnaires data.

Characteristics	Male			Female		
	Mean (SD)	Min	Max	Mean (SD)	Min	Max
Age (years)	22.71 (3.03)	18	30	22.75 (2.78)	18	29
Physical activity (MET-min/week)	2177.11 (1391.83)	66	7224	2544.78 (1475.21)	462	6813
Mind wandering	16.86 (4.92)	5	28	16.59 (5.08)	8	29

gyrus did not survive from multiple comparison correction in both low and high mind wandering groups.

Discussion

The current study aimed to examine whether mind wandering modulated the relations between physical activity and hippocampal functional connectivity. First, we found that mind wandering was negatively related to the resting-state functional connectivity between hippocampus and right inferior occipital gyrus. Additionally, we found there was significant interaction between physical activity and mind wandering in predicting the resting-state hippocampal functional connectivity at left precuneus, precentral gyrus, left superior frontal gyrus, and right medial frontal gyrus. Specifically, for participants with higher level of mind wandering, there was negative relation between physical activity and hippocampal functional connectivity at left precuneus and right precentral gyrus. For participants with lower level of mind wandering, physical activity was positively related to hippocampal functional connectivity at right medial frontal gyrus and bilateral precentral gyrus. These findings supported our hypothesis that mind wandering modulated the relations between physical activity and hippocampal functional connectivity.

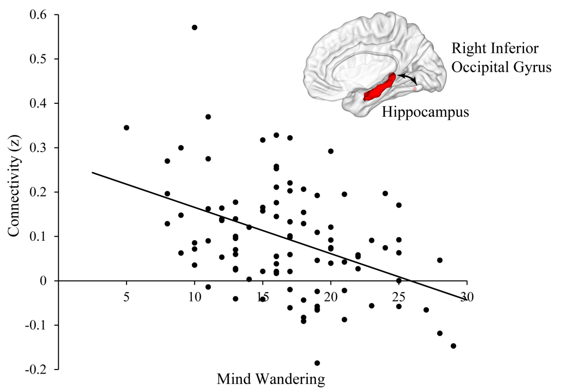

FIGURE 1
Mind wandering was negatively correlated with functional connectivity between hippocampus and right inferior occipital gyrus.

Interactions between physical activity and mind wandering in hippocampal functional connectivity

Our study found the significant interaction between physical activity and mind wandering in predicting hippocampal functional connectivity at left precuneus, right medial frontal gyrus, and bilateral precentral gyrus. These brain regions, similar to hippocampus, are closely related to physical activity or/and mind wandering (Schneider et al., 2009; Vago and David, 2012; Boccia et al., 2015; Christoff et al., 2016; Thielen et al., 2016). For example, the DMN, which includes precuneus and medial frontal gyrus as nodes, has been shown to be positively activated during mind wandering (Buckner et al., 2008; Andrews-Hanna, 2011). Additionally, a meta-analysis study showed that compared with controls, the meditators, who would experience more mind wandering, had greater activation in precuneus, precentral gyrus, and medial frontal gyrus during meditation (Boccia et al., 2015).

Meanwhile, numerous studies also found that during both resting and task states, people with higher physical activity or fitness showed greater activation at precuneus, precentral gyrus, and medial frontal gyrus than people with lower physical activity or fitness (Casey et al., 2000; Schneider et al., 2009; Voelcker-Rehage et al., 2010; Smith et al., 2011; Kimura et al., 2013; Thielen et al., 2016). For example, compared to the controls, people who received aerobic physical activity intervention showed greater activation at precuneus (Thielen et al., 2016), precentral gyrus (Voelcker-Rehage et al., 2010; Smith et al., 2011), and medial frontal gyrus (Casey et al., 2000; Kimura et al., 2013) during performing tasks that were highly demanding. Altogether, previous studies suggest that left precuneus, right medial frontal gyrus, and bilateral precentral gyrus may co-activate with hippocampus to support mind wandering and the functions of these brain regions may also be influenced by physical activity.

Furthermore, we found that the relations between physical activity and hippocampal functional connectivity vary as a function of mind wandering level. Previous studies have

TABLE 2 Interactions between physical activity and mind wandering.

Regions	Hemisphere	*F*	Cluster size	Peak MNI coordinates		
				x	y	z
Precuneus	left	21.925	113	−38	−65	36
Precentral gyrus	left	21.753	104	−35	12	41
Precentral gyrus	right	23.427	56	22	25	46
Superior frontal gyrus	bilateral	15.568	33	2	40	36
Medial frontal gyrus	right	17.104	33	−8	32	58

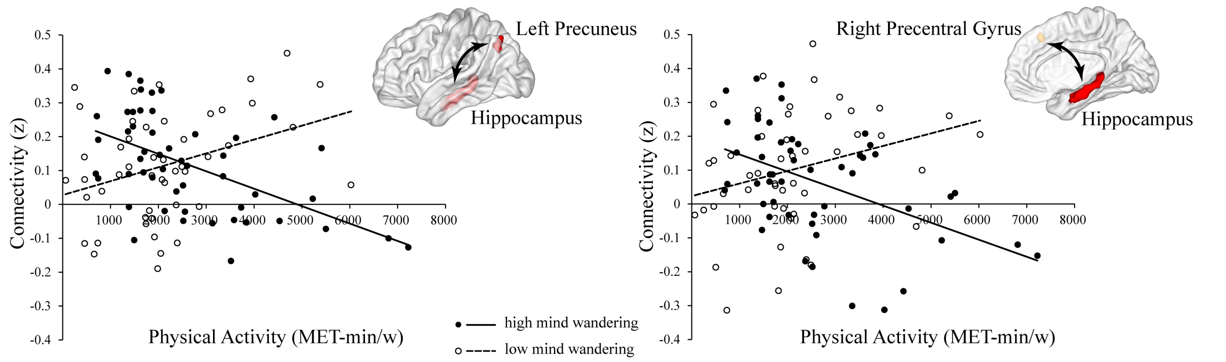

FIGURE 2
Negative relations between physical activity and hippocampal functional connectivity at left precuneus and right precentral gyrus in high mind wandering group.

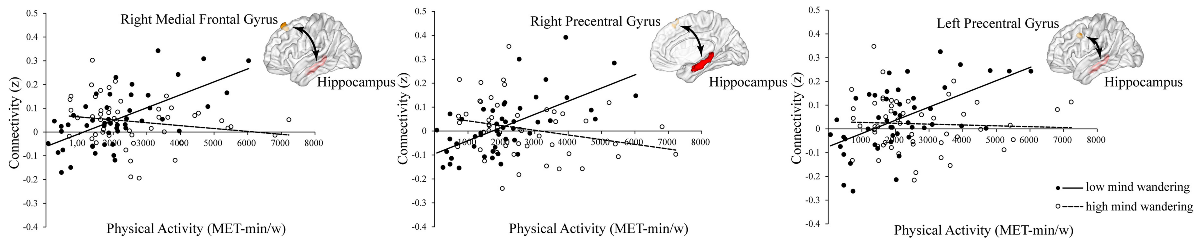

FIGURE 3
Positive relations between physical activity and hippocampal functional connectivity at right medial frontal gyrus, right precentral gyrus, and left precentral gyrus in low mind wandering group.

TABLE 3 Mind wandering modulated the relationship between physical activity and hippocampal functional connectivity.

	Z	Cluster size	Peak MNI coordinates			Polarity
			x	y	z	
Regions showing significant connectivity in high mind wandering group (*N* = 48)						
Left precuneus	−3.974	38	−38	−63	38	-
Right precentral gyrus	−4.026	26	25	30	46	-
Regions showing significant connectivity in low mind wandering group (*N* = 51)						
Right medial frontal gyrus	4.553	69	−8	35	56	+
Right precentral gyrus	3.988	52	22	20	61	+
Left precentral gyrus	4.489	33	−35	12	38	+

indicated that maintaining appropriate mind wandering level is critical in our daily life (Smallwood and Andrews-Hanna, 2013). Too much mind wandering may cause us to be dissociated from the external environment, which may result in deteriorated task performance, such as the performance in working memory task (McVay and Kane, 2010) and reading comprehension task (Smallwood et al., 2008; Unsworth and McMillan, 2013). However, a certain amount of mind wandering is also beneficial in some situations. For example, we also benefit from mind wandering in tasks or environments that require divergent thinking, such as creativity (Baird et al., 2012), problem solving (Smeekens and Kane, 2016), and successful management of long-term goals (Smallwood et al., 2013). Therefore, mind wandering enables us to reach balance in allocating attention to processing internal and external stimuli.

Previous studies also indicated that physical activity is related to the allocation of attentional resources (Hillman et al., 2006; Luque-Casado et al., 2015; Stillman et al., 2018). For example, physical activity had a larger effect on behavioral performance during task switch vs. repeat (Hillman et al., 2006), suggesting that physical activity affects the processing of information in tasks that have great demands on attentional resource (Kramer et al., 1999; Colcombe and Kramer, 2003). Additionally, another ERP study indicated that fitness was positively related to the neuroelectric activity that measures sustained attention, suggesting that individuals with higher fitness are more capable of allocating attentional resources over time (Luque-Casado et al., 2015).

Therefore, in terms of the findings that individuals with high vs. low mind wandering showed opposite relations between physical activity and hippocampal functional connectivity, we propose that physical activity may help individuals maintain appropriate level of mind wandering through affecting the interactions between hippocampus and other brain regions. Specifically, for people with lower level of mind wandering, physical activity may help intensify the functional connectivity between brain regions within networks of mind wandering. In contrast, for people with higher level of mind wandering, physical activity may reduce the connectivity between regions of brain networks that support mind wandering (Stillman et al., 2018). Although such interpretation needs more studies to verify, we further propose that when physical activity is considered as a kind of "medicine," individual differences are important to consider. In other words, the effect of physical activity may vary substantially between different people.

Main effect of mind wandering at inferior occipital gyrus

We found that mind wandering level was associated with the functional connectivity between hippocampus and right inferior occipital gyrus. The occipital gyrus participates in processing visual information and has been suggested to be important for object recognition (Gauthier et al., 2000; Sato et al., 2014; Jacques et al., 2019). Visual information is preliminarily processed and integrated in inferior frontal gyrus and then reprocessed in higher-level cognitive systems, such as the memory center for which hippocampus is a critical structure (Stone, 1983; Eichenbaum et al., 1992; Andersen et al., 2006). It has been suggested that compared to people with lower level of mind wandering, people with higher level of mind wandering focus more on processing internal information, but ignore external information or process it at superficial level without sending them to higher-order cognitive systems (i.e., hippocampal memory system) (Hasenkamp et al., 2012). As a result, for people with higher level of mind wandering, the connectivity between hippocampus and inferior occipital gyrus may become weaker compared to the ones with lower level of mind wandering.

Strengths and limitations

Previous studies showed that physical activity, hippocampal function, and mind wandering were related to each other. Our study contributed to establishing the modulating role of mind wandering in the relations between physical activity and resting-state hippocampal functional connectivity. However, the current study still had several limitations. First, the study design did not allow us to test the causal relations between physical activity, mind wandering, and hippocampal functions. Additionally, physical activity and mind wandering were measured by self-reported, which is subjective and maybe biased (Randy et al., 2003). Therefore, future studies need to include more objective measurements and use study designs that allow us to test the causal effect of physical activity on mind wandering and the related brain functions.

Conclusion

To summarize, this study established the modulating role of mind wandering on the relations between physical activity and resting-state hippocampal functional connectivity at precuneus, precentral gyrus, and medial frontal gyrus. Specifically, for individuals with higher level of mind wandering, physical activity was negatively related to hippocampal functional connectivity at left precuneus and right precentral gyrus; in contrast, for individuals with lower level of mind wandering, physical activity was positively related to hippocampal functional connectivity at right medial frontal gyrus and bilateral precentral gyrus. We interpreted such findings as that physical activity may help maintain an appropriate level of mind wandering by affecting the interaction between hippocampus and other brain regions. Therefore, the current study provides insight into the variations between individuals on the relations between physical activity and brain functions, implying that individual differences are important to consider when we aim to maintain or improve neurocognitive health through increasing physical activity.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by Zhejiang University. The patients/participants provided their written informed consent to participate in this study.

Author contributions

DS drafted the initial manuscript, carried out data analysis, interpreted results, and critically revised the manuscript for important intellectual content. FG conceived and designed the study, contributed to acquisition, analysis and interpretation of the data, drafted, reviewed, and critically revised the manuscript for important intellectual content. XH contributed to data collection and critically revised the manuscript for important intellectual content. KH and YH contributed to conception of the study and critically revised the manuscript for important intellectual content. All authors approved the final manuscript as submitted.

Funding

This work was supported by the MOE (Ministry of Education in China) Project of Humanities and Social Sciences (20YJA190002), National Natural Science Foundation of China (General Program; 81971245), and the Fundamental Research Funds for the Central Universities.

Acknowledgments

We thank our participants and research assistants. Especially, we also thank Jiawen Zhang and Binyu Teng for helping with data collection.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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Frontiers in Human Neuroscience

TYPE Systematic Review
PUBLISHED 09 February 2023
DOI 10.3389/fnhum.2023.854515

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OPEN ACCESS

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SPECIALTY SECTION
This article was submitted to Cognitive Neuroscience, a section of the journal Frontiers in Human Neuroscience

RECEIVED 14 January 2022
ACCEPTED 19 January 2023
PUBLISHED 09 February 2023

CITATION
Wen J, Leng L, Hu M, Hou X and Huang J (2023) Effects of whole-body vibration training on cognitive function: A systematic review. *Front. Hum. Neurosci.* 17:854515.
doi: 10.3389/fnhum.2023.854515

Effects of whole-body vibration training on cognitive function: A systematic review

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Background: Whole-body vibration (WBV) training is a novel training method that stimulates the human neuromuscular system by the use of vibration, the frequency and amplitude of which are controlled, thereby inducing adaptive changes in the body. WBV training is widely used as a clinical prevention and rehabilitation tool in physical medicine and neuro-rehabilitation as a clinical prevention and rehabilitation tool.

Objectives: The aim of the present study was to review the effects of WBV on cognitive function, provide an evidence-based foundation for future research on WBV training, and promote additional popularization and use of the methodology in clinical practice.

Methods: A systematic review of articles extracted from the following six databases was conducted: PubMed, Web of Science, China National Knowledge Infrastructure, Embase, Cochrane, and Scopus. A literature search was performed on articles in which the effects of WBV on cognitive function were evaluated.

Results: Initially, a total of 340 studies were initially identified, among which 18 articles that satisfied the inclusion criteria were selected for inclusion in the systematic review. Participants were allocated into two groups: patients with cognitive impairment and healthy individuals. The results demonstrated that WBV was both positive and ineffective in its influence on cognitive function.

Conclusion: The majority of studies suggested that WBV may be a useful strategy for the management of cognitive impairment and should be considered for inclusion in rehabilitation programs. However, the impact of WBV on cognition requires additional, larger, and adequately powered studies.

Systematic review registration: https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=376821, identifier CRD42022376821.

KEYWORDS

whole-body vibration, cognitive function, rehabilitation, cognitive ability, vibration training

Abbreviations: WBV, whole-body vibration; MS, multiple sclerosis; CNKI, China National Knowledge Infrastructure; CWIT, Color-Word Interference Test; DSBT, Digit Span Backward task; ADHD, attention deficit hyperactivity disorder; ImPACT, immediate postconcussion assessment and cognitive test; HRQoL, health-related quality of life; PASAT-3, Paced Auditory Serial Addition Test; MMSE, Mini-Mental State Examination; EEG, electroencephalogram; WBVT, whole-body vibration training; STP-TBAG, Stroop Test TBAG (Scientific and Technological Research Council of Turkey); BRIEF, Behavior Rating Inventory of Executive Function; CMMSE, Cantonese Mini-Mental State Examination; SWV, Sonic Wave Vibration.

Introduction

Whole-body vibration (WBV) training is a method of neuromuscular training which produces oscillations that are transferred to the body and perceived by the muscular-skeletal apparatus (Kim and Lee, 2018; Fereydounnia and Shadmehr, 2020). At the end of the 19th century, this method was first used by Goetz (2009) to treat gait disorders in patients with neurological disabilities, especially those with Parkinson's disease. WBV may be conducted when a subject either stands stationary (passive exercise) or performs movements while standing, sitting or lying on the vibration platform (active exercise). In the study by Stania et al. (2016) and Pang et al. (2013), subjects performed specific exercise training on the vibration platform, which was considered active WBV training. However, in the articles highlighted in the current review, WBV training was conducted by asking subjects to sit on a bench on a vibrating platform or stand directly on the platform. In the study by Amonette et al. (2015), a static squatting position was adopted using 45° of knee flexion. Here, the body was moving (with reflexive muscle contractions) without active intervention, which was considered a form of passive physical exercise (Fereydounnia and Shadmehr, 2020). Moreover, the mechanical load caused was extremely limited, and was considered safe, allowed for ready adjustment, and ease of use. Therefore, it was general recommended for patients who were weak, untrained, or had defective balance problems.

Cognitive functioning refers to the ability of the human brain to process, store and extract information, that is, the capability to process the occurrence and development of a series of events (Naito et al., 2000). Cognitive functioning includes many independent areas, such as memory, attention, executive ability, feeling, perception, thinking, learning, and judgment. When one or more of the above mentioned functions are impaired, the patient is considered to suffer from cognitive impairment.

After detailed observation, it was concluded that exercise can improve functional activity in the prefrontal cortex, the superior cortex of the central axis, and the marginal cortex. Overall, exercise can improve cognitive functioning (Kingwell, 2019). In accordance with the specific principles of exercise, the benefits of different methods are not equivalent and the relationship between different styles, such as aerobic and resistance exercise, with cognitive capability has been confirmed in previous studies (Karssemeijer et al., 2017; Herold et al., 2019; Moriarty et al., 2019; Stern et al., 2019). However, few studies have been published that have evaluated the relationship between WBV and cognitive function. In 2014, to ascertain the effects of WBV therapy on cognitive functioning in healthy young individuals, Regterschot et al. (2014) treated participants by performing WBV training and concluded that WBV training had a positive short-term effect on executive function in these adults. In Rosado et al. (2021) conducted a randomized controlled trial and found that psychomotor intervention combined with WBV training was effective in preventing falls, cognitive function and physical function decline. However, Santin-Medeiros et al. (2017) believed that 8 months of WBV training in elderly women did not improve the cognitive status. Lam et al. (2018) proposed that WBV training combined with a routine activity program had no significant effect on the cognitive ability of patients with mild or moderate dementia. Furthermore, no systematic reviews are available that have established an association between WBV training and cognitive function. In addition, a clear consensus regarding vibration exposure parameters (i.e., frequency, amplitude, or duration) has not been reached. Hence, the purpose of this systematic review was to review the available literature and critically observe the effect of WBV training on cognitive function.

Materials and methods

Search strategy

PubMed, Web of Science, China National Knowledge Infrastructure (CNKI), Embase, Cochrane, and Scopus databases were used to comprehensively and systematically search the literature for articles published prior to December 2021, with no limit on the earliest date. According to the PICO policy, keywords including ["whole-body vibration" or "vibration training" (Title/Abstract)] AND ["cognitive function" or "cognitive control" or "cognitive ability" or "cognition" (Title/Abstract)] were used. The search was limited to full original articles that focused on human subjects without restrictions in the language of publication. The manuscript adheres to the PRISMA guidelines for reporting systematic reviews (Page et al., 2021).

Inclusion and exclusion criteria

Articles that met the following criteria were selected: meta-analyses, systematic reviews, or experimental research related to WBV training, at least one outcome of the study was related to cognitive function.

Articles were excluded if any of the following exclusion criteria applied: WBV training studies not in a sports or medical field, such as agriculture, construction, transportation, and mechanics; studies focused on the detrimental effects of mechanical vibration in the work environment, for example, when operating tools (e.g., sledgehammers or forming machines) or while riding vehicles (e.g., trucks, helicopters, or tanks); an abstract or conference paper; studies in which WBV was not utilized; participants were not human, for example, animal studies.

Data collection and analysis

To assess the effects of WBV training on cognitive function and record the principal characteristics of each study, a standardized data extraction and evaluation form developed by the authors was used to record relevant data. Characteristics of the studies included first author, publication year, target population, number of participants, intervention and control groups, outcomes, and WBV specifications. In accordance with the guidelines of van Heuvelen et al. (2021), the WBV specifications included the type of vibration, frequency, amplitude of WBV, duration, and posture. Details of the data extraction process are displayed in **Table 1**.

For quantitative analysis, it was found that different studies used different methods to evaluate the data. Four articles used the MMSE scale to measure the main results, whereas six articles used the Stroop Test. The MMSE scale and the Stroop Test are suitable for the use of Review Manager version 5.4 for quantitative analysis. **Figure 1** shows forest map of the effect estimation and comparison of the MMSE scale. **Figure 2** shows forest map of the effect estimation and comparison of the Stroop Test.

TABLE 1 Effects of whole-body vibration (WBV) training on cognitive function in humans.

References	Participants	Groups	Frequency and amplitude of WBV	Duration of WBV	Outcome measures	Outcomes
Fereydounnia and Shadmehr, 2020	15 women with normal lordosis and 15 women with lumbar hyper-lordosis	Experimental group: women with lumbar hyper-lordosis ($n = 15$) Control: women with normal lordosis ($n = 15$)	Frequency: 30 Hz, high range: 5 mm	5 times (1 min each)	SART test system	WBV had positive immediate effects on the reaction time in both groups, but it had negative effects on anticipatory skill with high speed in women with normal lumbar lordosis.
Kim and Lee, 2018	18 senile women with suspected mild dementia	Experimental group: WBV ($n = 9$) Control group: no vibration ($n = 9$)	Frequency: 20–40 Hz, amplitude: 3 mm	5 days/week, 8 weeks	EEG, MMSE	WBV training activated the cerebrovascular circulation, having a positive impact on cognitive functioning.
Regterschot et al., 2014	133 healthy participants (112 females, 21 males)	Treatment: WBV ($n = 133$)	Frequency: 30 Hz, amplitude: 0.5 mm	6 times (2 min each)	CBT, CWIT, SDS, DSBT	WBV had a short-term positive effect on executive function (attention and inhibition) in young people.
Rosado et al., 2021	51 participants (aged 75.4 ± 5.6 years)	EG1: psychomotor intervention program ($n = 16$) EG2: psychomotor intervention program + WBV ($n = 16$) Control: daily activities($n = 19$)	Frequency: 12.6–15 Hz, amplitude: 3 mm	3 times/week (3–6 min each), 24 weeks	CogTUG	Psychomotor intervention combined with WBV training is effective in preventing falls, cognitive function and physical function decline.
Santin-Medeiros et al., 2017	37 women	Treatment: WBV ($n = 19$) Control: no vibration ($n = 18$)	Frequency: 20 Hz, amplitude: 2 mm	2 times/week (30–35 min each), 8 months	Abbreviated mental test	WBV training did not improve HRQoL scores, life satisfaction, cognitive status or fall risk in elderly women.
Lam et al., 2018	54 elderly adults (40 women) with mild or moderate dementia	Experimental group: WBV ($n = 27$) Control group: usual routine ($n = 27$)	Frequency: 30 Hz, amplitude: 2 mm	2 times/week, 9 weeks	CMMSE	No significant difference in CMMSE score or changes in outcomes measured at post-training and at 3-month follow-up identified.
den Heijer et al., 2015	55 healthy children (aged 8–13)	Treatment: WBV ($n = 55$)	Frequency: 30 Hz, amplitude: 0.44–0.6 mm	3 min	The Stroop Color-Word Interference Test	WBV training improved the inhibitory function of children, with a therapeutic effect related to intelligence and age, but not to ADHD.
Amonette et al., 2015	12 healthy participants (8 men and 4 women)	VV: vertical vibration ($n = 12$) RV: rotational vibration ($n = 12$) Control: placebo ($n = 12$)	Frequency: 30 Hz, amplitude: 4 mm	5 times (2 min each)	ImPACT	An acute bout of static squats with a 45° angle of knee flexion accompanied by WBV did not affect visual or verbal memory, reaction time, or impulse control measured using ImPACT, but motor processing speed may have been increased after vertical vibration.
de Bruin et al., 2020	Seventeen elderly adults (10 women, 7 men)	Treatment: WBV ($n = 9$) Control: placebo ($n = 8$)	Frequency: various, amplitude: 3 mm	5 times (1 min each), 3 days/week, 8 weeks	TMT-A, TMT-B	8-week SR-WBV combined with EXDT intervention had a positive effect on physical function and cognition of the care-dependent elderly.
Dennis et al., 2008	A 25-year-old patient with ADHD and 6 healthy college students	Treatment: WBV (a 25-year-old patient with ADHD) ($n = 1$) Control: no vibration (6 healthy college students) ($n = 6$)	Frequency: 30 Hz, amplitude: 0.44–0.66 mm	10 consecutive days, 3 times/day (15 min each)	TAP, Digit Span Backward task, Stroop Color-Word Interference task, controlled oral word association test, items drawn from the attention questionnaire	Both ADHD patient and healthy individuals showed significant improvement in attention, memory, and divergent thinking.

(Continued)

TABLE 1 (Continued)

References	Participants	Groups	Frequency and amplitude of WBV	Duration of WBV	Outcome measures	Outcomes
Cabeza et al., 2004	17 patients with ADHD and 83 healthy individuals	Treatment: WBV ($n = 100$)	Frequency: 30 Hz, amplitude: 0.44–0.66 mm	2 min	the Stroop Color-Word Interference task	Both ADHD patients and healthy individuals showed significant improvements in attention.
Yang et al., 2016	25 adults with MS	Treatment: WBV ($n = 25$)	Frequency: 20 Hz, amplitude: 1.3 mm	5 times/day (1 min each), 3 days/week, 8 weeks	PASAT-3″	Cognitive functioning in MS patients was enhanced.
Uhm and Yang, 2018	30 patients with stroke diagnosed within 3 months	Group I: WBV + BPCT ($n = 10$) Group II: AS + BPCT ($n = 10$) Group III: BPCT ($n = 10$)	NR	8 weeks	EEG	WBV combined with computerized postural control training improved muscle and cerebral cortex activity in stroke patients.
Durgut et al., 2020	30 children (7–11 years of age) with ADHD	Group I: TT ($n = 15$) Group II: TT + WBV ($n = 15$)	Frequency: 50 Hz, amplitude: 0–5 mm	3 days/week, 8 weeks (15 min each)	STP-TBAG, BRIEF	TT + WBWT training improved the scores of Stroop test, BRIEF, CRS, PedsQL, and TBAG Form.
Odano et al., 2022	16 patients with aMCI (aged 63.5 ± 8.2 years), 7 men and 9 women	Treatment: WBV ($n = 16$)	Frequency: 35–40 Hz, amplitude: NR	2 times/week (20 min each), 24 weeks	rCBF	WBV exercise and training increase rCBF in aMCI patients, and WBV training enhances cognitive function and may increase the cognitive reserve.
Zhu, 2016	90 male patients with myasthenia	TC: tai chi ($n = 24$) WBV: WBV ($n = 28$) Control: no WBV ($n = 27$)	Frequency: 12–16 Hz, amplitude: 3–5 mm	5 times/day (1 min each), 5 days/week, 8 weeks	MMSE	WBV training had no effect on the MMSE score of cognitive ability compared with the control group.
Boerema et al., 2018	34 humans randomly assigned to a WBV or control group	Treatment: WBV ($n = 18$) Control: no vibration ($n = 16$)	Frequency: 30 Hz, amplitude: 0.5–1 mm	Humans: 4 days/week (4 min each), 5 weeks	The Stroop Test, digit memory span forward/backward, TMT	Cognitive tests in humans revealed a selective improvement in the Stroop Color-Word test after WBV training.
Choi and Mizukami, 2020	24 participants (aged 88.0 ± 5.0 years)	Treatment: SWV ($n = 13$) Control: no SWV ($n = 11$)	NR	5 days/week, 2 months (10 min each)	MMSE, NIRS	The score of MMSE in SWV group was improved, and the brain NIRS also showed that the concentration of oxidized hemoglobin and total hemoglobin increased significantly.

ADHD, attention deficit hyperactivity disorder; aMCI, amnestic mild cognitive impairment; AS, aero-step; BPCT, computerized postural control training; BRIEF, Behavior Rating Inventory of Executive Function; CBT, the Stroop Color-Block Test; CMMSE, Cantonese Mini-Mental State Examination; CogTUG, cognitive TUG test; CRS, Conners' rating scale; CWIT, Stroop Color-Word Interference Test; DSBT, Digit Span Backward task; HRQoL, health-related quality of life; ImPACT, immediate postconcussion assessment and cognitive test; MMSE, Mini-Mental State Examination; MS, multiple sclerosis; NR, not reported; PASAT-3″, Paced Auditory Serial Addition Test-3 Seconds; PedsQL, pediatric quality of life inventory; rCBF, regional cerebral blood flow; SART, speed anticipation reaction time; SDS, stroop difference score; SWV, Sonic Wave Vibration; STP-TBAG, Stroop Test TBAG form; TAP, test battery of attentional performance; TMT, trail making test; TT, treadmill training; WBVT, whole body vibration training.

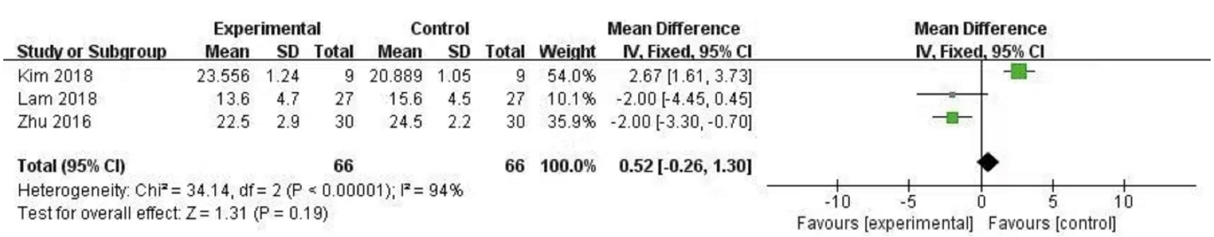

FIGURE 1
Forest plot of MMSE scale.

Quality assessment

The methodological quality of the included articles was assessed by two independent raters using the standardized and validated Physiotherapy Evidence Database (PEDro) scale for quality. The PEDro scale was used to evaluate the scientific rigor of the selected clinical trials (9–10 = excellent, 6–8 = good, 4–5 = fair, and ≤4 = poor) (Centre for Evidence-Based Physiotherapy, 2015). The

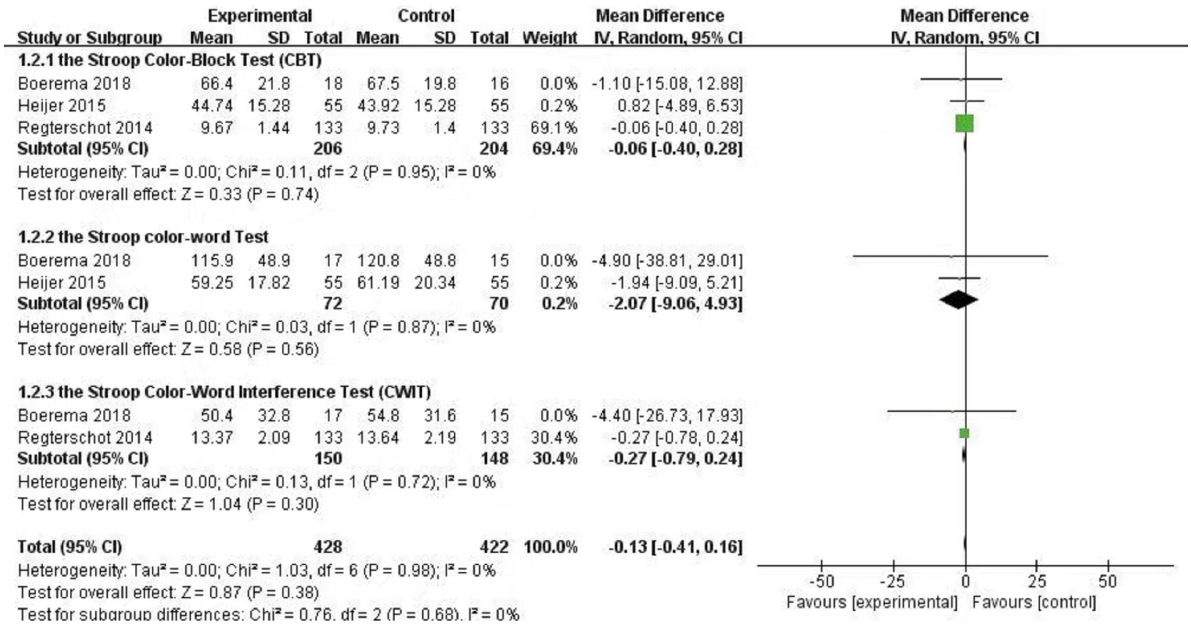

FIGURE 2
Forest plot of the Stroop Test.

PEDro scale is an 11-item scale that has previously been used in systematic reviews (Cashin and McAuley, 2020). The results of the assessment of the PEDro scale are presented in **Table 2**.

The risk of bias was assessed by collaboration of the two reviewers, and disagreements were resolved by discussion. To evaluate the methodological quality, the criteria of the Cochrane risk of bias tool were used.

Registration and protocol

Systematic review was performed using the preferred reporting items for the PRISMA checklist. This review was registered in the PROSPERO database (Registration Number: CRD42022376821).

Results

Study selection

After searching the electronic databases PubMed, Scopus, CNKI, Embase, Cochrane, and Web of Science, 340 potential relevant studies were identified. After removing duplicates, 147 articles remained. In accordance with the inclusion and exclusion criteria, 204 articles were excluded, mostly because the focus was on vibration in agriculture, construction, transportation, and machinery, rather than WBV training related to the sports or medical field. After reading the abstracts, followed by the full text of the articles, 18 studies ultimately satisfied the inclusion criteria and were included in the systematic review. The process for literature screening is displayed in **Figure 3**. The results of the Pedro scale are presented in **Table 2**. Articles were managed using Endnote software.

All 18 articles were thoroughly analyzed and approved by two reviewers using the PEDro scale. **Figure 4** shows the risk of bias for each of the included studies. Only one study used a randomized tool for sealing envelopes, and 10 studies mentioned random sequence generation, but did not include information regarding blindness of assessors.

The GRADE was used to assess the certainty of evidence. After completion of the classification of evidence, a summary of evidence and results is presented in **Table 3**.

Effect of WBV on the cognitive ability of individuals with normal cognition

Cognition refers to the process of acquisition, coding, operation, extraction, and the use of sensory input information, a psychological process between input and output, including perception, attention, memory, and thinking. The cognitive level in different social groups differs. Therefore, studies have been conducted on healthy individuals or those with sub-optimal health but with normal cognition, such as healthy children, elderly women, and women with lumbar hyper-lordosis.

To ascertain the effects of WBV therapy on cognitive functioning in healthy young individuals, in Regterschot et al. (2014) recruited 133 healthy youths (112 females, 21 males) with a mean age of 20.5 ± 2.2 years to undergo WBV treatment at 30 Hz with an amplitude of approximately 0.5 mm for 2 min, 6 times. The results indicated that Stroop Color-Word Interference Test (CWIT) scores improved, but Digit Span Backward task (DSBT) scores remained unchanged. Finally, it was concluded that 2 min of passive WBV training had a positive short-term effect on executive function (attention and inhibition) in young adults. Subsequently, den Heijer et al. (2015) found showed that 3 min of WBV training at 30 Hz with an amplitude of 0.44–0.6 mm improved the inhibitory function of healthy children, with a therapeutic effect related to intelligence and age, but not to attention deficit hyperactivity disorder (ADHD).

TABLE 2 Study quality using the PEDro scale.

References	1*	2	3	4	5	6	7	8	9	10	11	Total
den Heijer et al., 2015	1			1				1		1	1	4
Cabeza et al., 2004	1			1				1	1	1	1	5
de Bruin et al., 2020	1			1				1		1	1	4
Yang et al., 2016	1			1				1		1	1	4
Kim and Lee, 2018	1			1				1	1	1	1	5
Uhm and Yang, 2018	1	1		1	1			1	1	1	1	7
Durgut et al., 2020	1	1	1	1	1	1	1	1	1	1	1	10
Lam et al., 2018	1	1		1	1	1	1	1	1	1	1	9
Zhu, 2016	1	1		1	1			1	1	1	1	7
Regterschot et al., 2014	1			1				1		1	1	4
Choi and Mizukami, 2020	1	1		1	1			1	1	1	1	7
Amonette et al., 2015	1	1		1				1	1	1	1	6
Fereydounnia and Shadmehr, 2020	1			1				1	1	1	1	5
de Bruin et al., 2020	1	1		1	1	1	1	1	1	1	1	9
Santin-Medeiros et al., 2017	1	1		1				1	1	1	1	6
Boerema et al., 2018	1	1		1	1	1	1	1	1	1	1	9
Rosado et al., 2021	1	1		1	1			1	1	1	1	7
Odano et al., 2022	1			1				1		1	1	4

1, eligibility criteria and source of participants; 2, random allocation; 3, concealed allocation; 4, baseline comparability; 5, blinded participants; 6, blinded therapists; 7, blind assessors; 8, adequate follow-up; 9, intention-to-treat analysis; 10, between-group comparisons; 11, point estimates and variability.
*Item 1 does not contribute to the total score.

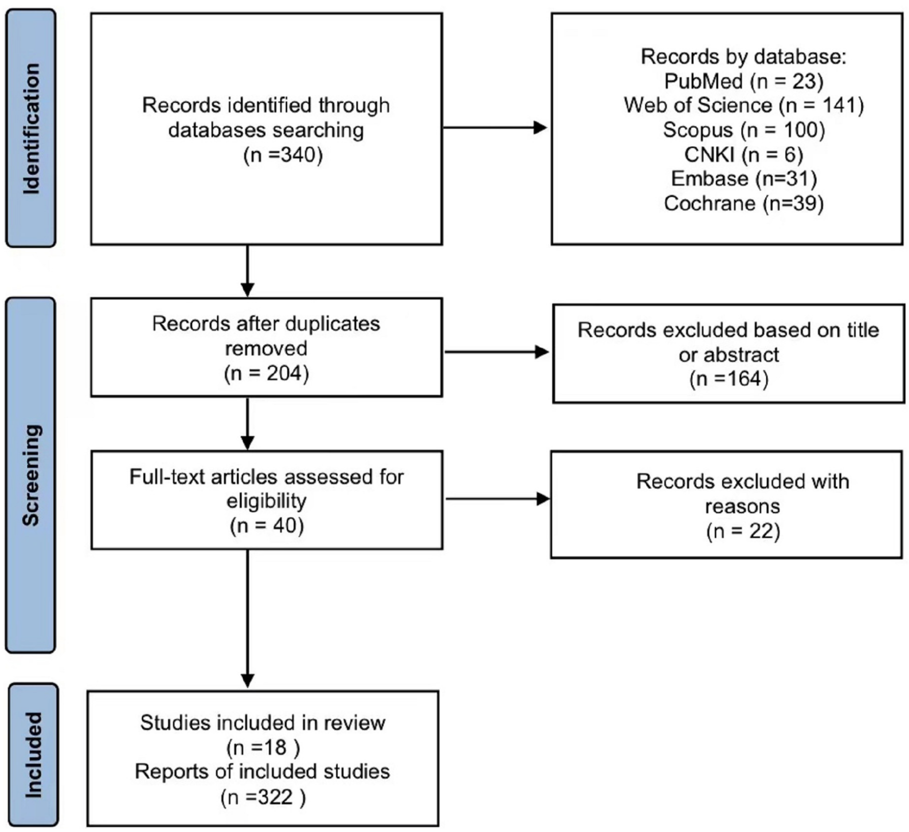

FIGURE 3
Flowchart representing the process of article selection.

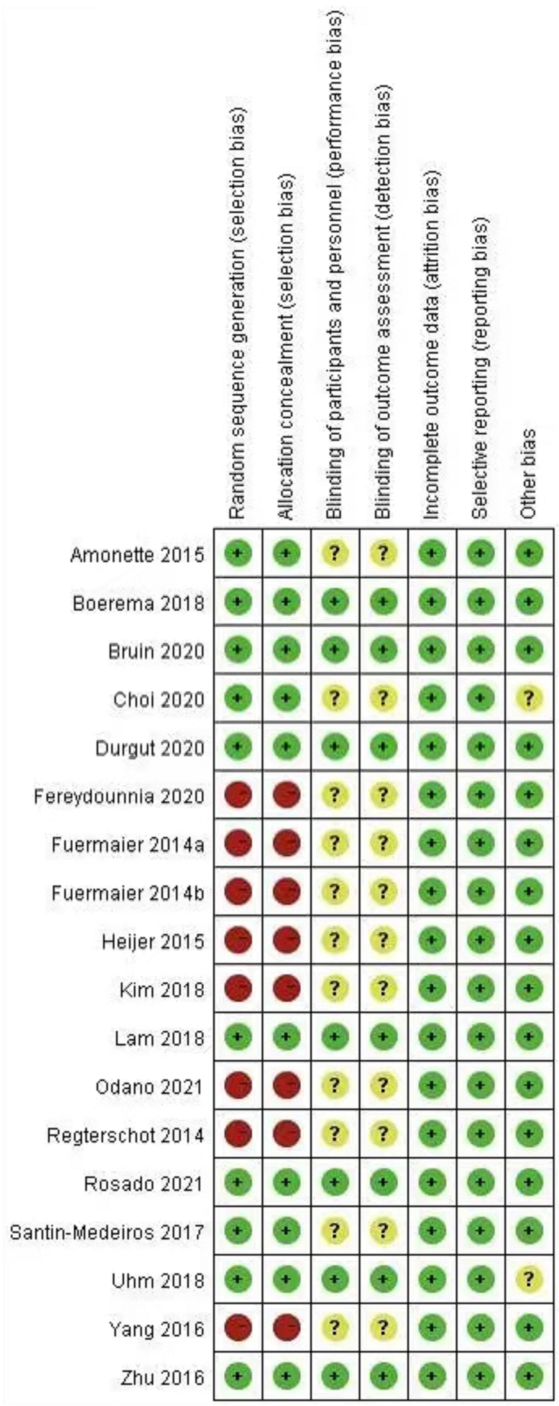

FIGURE 4
Risk of bias summary.

In the same year, Amonette et al. (2015) recruited 12 healthy subjects for WBV exercise at 30 Hz with a 4-mm amplitude (2 min each, 5 times) to determine whether WBV exercise reduced neurocognition in healthy subjects. The results indicated that WBV training with knee flexion at a 45° angle did not affect visual or verbal memory, reaction time, or impulse control measured using the Immediate Post-concussion Assessment and Cognitive Test (ImPACT), although motor processing speed may increase following vertical vibration. It is worth noting that the study performed by Amonette et al. (2015) emphasized body posture during WBV, with static squats using a squatting angle of 45°. The present review demonstrated an association between slow psychomotor reaction time and lower back pain, with a correlation between lumbar hyper-lordosis and lower back pain. In neurocognitive tests, the choice of reaction time represents an important reference index. In Fereydounnia and Shadmehr (2020) conducted passive WBV training (frequency = 30 Hz, amplitude = 5 mm, duration = 5 min) training on 15 women with normal lumbar lordosis and 15 women with hyper-lordosis of the lumbar spine. The data demonstrated that WBV training had an immediate positive effect on reaction time in both groups, but a negative effect on anticipatory skills with high speed in women with normal lumbar lordosis.

As age increases, physiological functioning in humans gradually declines, and is combined with changes in cognitive functioning. Brain imaging studies have suggested that brain volume changes faster in adults over the age of 50, with an annual decline of 0.35% compared with 0.12% in young individuals. Brain volume has been confirmed to positively correlate with cognitive function (Cabeza et al., 2004; Dennis et al., 2008). In de Bruin et al. (2020) randomly divided 17 elderly individuals into two groups: an intervention group ($n = 9$) and a sham operation group ($n = 8$). The intervention group received 4 weeks of WBV training (1 min each, 5 times, 3 days/week). From weeks 5 to 8, a passive trampoline program of 5 min was introduced following the vibration sessions. The results indicated that the 8-week training program, consisting of a combination of stochastic resonance WBV and exergame-dance training, was beneficial to both physical and cognitive performance in older care home-dwelling adults. In the same year, to clarify the effect of Sonic Wave Vibration (SWV) on cognitive function and autonomic nervous function, Choi and Mizukami (2020) randomly divided 24 elderly patients into a SWV group and a control group. The SWV group received SWV for 10 min a day, 5 days a week for a total of 2 months. Compared with the control group, the MMSE score in the SWV group improved. In addition, the results of brain NIRS showed that the concentration of oxidized hemoglobin and total hemoglobin increased significantly, thereby suggesting that activation of frontal lobe function may be improved. Similarly, in Rosado et al. (2021) conducted a randomized controlled trial on 51 subjects with a mean age of 75.4 ± 5.6 years. Fifty-one participants were allocated into two experimental groups and a control group: EG1 was enrolled in a psychomotor intervention program, EG2 was enrolled in a combined exercise program (psychomotor intervention program and whole-body vibration program), and the control group maintained their usual daily activities. The vibration amplitude (mm) was always 3 and the frequency (Hz) increased from 12.6 to 15. Rosado et al. (2021) indicated that psychomotor intervention combined with WBV training was effective in preventing falls, cognitive function and physical function decline. However, Santin-Medeiros et al. (2017) did not concluded this. A total of 37 elderly women, with a mean age of 82.4 ± 5.7 years was randomly divided into two groups: vibration (n = 19) and control (n = 18) groups. WBV training for 8 months at 20 Hz with a 2-mm amplitude (30–35 min each, twice per week) did not improve health-related quality of life (HRQoL) scores, life satisfaction, cognitive status, or fall risk in elderly women. Inconsistencies in related research studies may be due to differences in the evaluation and testing methods. Santin-Medeiros et al. (2017) examined cognitive capability using intelligence tests. Both Santin-Medeiros and Zhu concluded that WBV training did not improve cognitive function, but there were multiple differences between the two subject types (male patients with myasthenia and elderly

TABLE 3 Evidence summary form of the GRADE.

Certainty assessment							Number of patients		Effect		Certainty	Importance
Number of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Whole-body vibration training	No whole-body vibration training	Relative (95% CI)	Absolute (95% CI)		
MMSE scale												
3	Randomized trials	Serious[a]	Not serious	Not serious	Not serious	None	66	66	–	MD **0.52 higher** (0.26 lower to 1.3 higher)	⊕⊕⊕◯ Moderate	CRITICAL
The Stroop Color-Block Test (CBT)												
4	Observational studies	Very serious[b]	Not serious	Not serious	Not serious	None	207	210	–	MD **0.06 lower** (0.4 lower to 0.28 higher)	⊕◯◯◯ Very low	IMPORTANT
The Stroop Color-Word Test												
2	Randomized trials	Serious[c]	Not serious	Not serious	Not serious	None	72	70	–	MD **2.07 lower** (9.06 lower to 4.93 higher)	⊕⊕⊕◯ Moderate	IMPORTANT
The Stroop Color-Word Interference Test (CWIT)												
3	Observational studies	Serious[c]	Not serious	Not serious	Not serious	None	151	154	–	MD **0.27 lower** (0.79 lower to 0.24 higher)	⊕◯◯◯ Very low	IMPORTANT

CI, confidence interval; MD, mean difference; MMSE, Mini-Mental State Examination; CBT, Color-Block Test; CWIT, Color-Word Interference Test. [a]Two articles showed that there was no significant change in the MMSE score of cognitive ability after WBV training. However, one article showed that there was significant change in the MMSE score of cognitive ability after WBV training. [b]The two articles were observational studies, which were not randomly grouped and not allocated or hidden. An article is a random assignment experiment, and allocation hiding was carried out. [c]One article was observational experiments, which was not randomly grouped and not allocated and hidden. An article is a random assignment experiment, and allocation hiding was carried out. GRADE Working Group grades of evidence. High certainty: We are very confident that the true effect lies close to that of the estimate of the effect. Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect. Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

10.3389/fnhum.2023.854515

women). Few studies that focused on the relationship between WBV and cognition have been published, the results of which are contradictory. The majority of studies have demonstrated that WBV training improved cognitive performance, with only a small number concluding that it does not.

Effect of WBV on the cognitive ability of patients with cognitive impairment

Cognitive impairment generally refers to problems with memory, attention, the learning of new information, planning, organization, and decision making. The degree of injury closely relates to the type of disease and its duration. Cognitive rehabilitation is a type of therapy that principally aims to improve attention, memory, and executive function (Chung et al., 2013).

The use of WBV training to ameliorate cognitive impairment was first proposed in 2014 when Fuermaier et al. (2014a) studied a 25-year-old patient with ADHD and 6 healthy college students with a mean age of 22.8 ± 2.4 years. It was found that 10 days of WBV treatment at 30 Hz with an amplitude of 0.44–0.66 mm improved attention, memory, and divergent thinking in both ADHD patients and healthy individuals. In the same year, Fuermaier et al. (2014b) continued to conduct in-depth research and verified these results using an increased sample size. A total of 83 healthy individuals aged 18–31 and 17 ADHD patients aged 21–28 underwent acute WBV training at 30 Hz with a 0.44–0.66 mm amplitude. The data showed that 2 min of WBV training improved attention in both healthy individuals and ADHD patients. Executive function refers to a group of cognitive processes involving attention, working memory, and cognitive flexibility, essential for higher-order mental functioning (Logue and Gould, 2014; Regterschot et al., 2014). Subsequently, to determine the effect of 8-weeks of WBV training on the extent of disabilities in patients with MS, Yang et al. (2016) exposed 25 MS patients with a mean age of 50.3 ± 14.1 years to 20 Hz vibrations with a 1.3-mm amplitude (1-min exposure to vibration in each group, 5 groups per day, 3 days per week, with a 1-min rest between groups). Patients were evaluated using a Paced Auditory Serial Addition Test (PASAT-3), a commonly used scale of cognitive scores, that included processing speed when evaluating auditory information, computing ability, continuous attention, and distraction. Yang et al. (2016) demonstrated significant changes in cognitive ability in MS patients. Finally, it was concluded that 8 weeks of controlled WBV training reduced the extent of disability in MS patients. PASAT-3 scores used by Yang et al. were not used in other studies to test the relationship between WBV training and cognition. Instead, a Stroop Test and Mini-Mental State Examination (MMSE) have been widely used in other studies. In Kim and Lee (2018) studied women with senile dementia aged 65 or above, and randomly divided them into vibration ($n = 9$) and control groups ($n = 9$) for 8 weeks of WBV training at 20–40 Hz. Finally, the data indicated that WBV training activated the cerebral cortex, which had a positive impact on cognitive functioning. In terms of cognitive assessment methods, Kim et al. used electroencephalograms (EEG). Uhm and Yang (2018) also observed the effects of 8 weeks of WBV training combined with computerized postural control training on the cognitive ability of 30 stroke patients within 3 months of diagnosis using EEG. The results showed that this mixed training method improved muscle and cerebral cortex activity in stroke patients. The studies performed by Kim et al. and Uhm et al. are the only two studies that used EEG to analyze cognitive function following WBV exercise intervention. To compare the effects of treadmill training (TT) and WBV training on attention, the severity of ADHD symptoms in patients, impairment of executive function behavior, and the quality of life in children with ADHD, Durgut et al. (2020) randomly allocated 30 children with ADHD into two groups: a "TT" group and "WBVT + TT" group. Both groups received TT for 8 weeks (3 days/week), and the "WBVT + TT" group received an additional 8 weeks of WBV training at 50 Hz at a 0–5 mm amplitude. The results demonstrated that TT + WBWT training improved the Stroop Test TBAG (Scientific and Technological Research Council of Turkey) (STP-TBAG) and Behavior Rating Inventory of Executive Function (BRIEF) scores. In recent study, Odano et al. (2022) conducted WBV training (frequency = 35–40 Hz, duration = 20 min) on 16 patients with amnestic mild cognitive impairment (aMCI). The results demonstrated that WBV exercise and training increased rCBF in aMCI patients. Moreover, WBV training enhanced cognitive function and may increase cognitive reserve.

Although the majority of studies demonstrated that WBV training improved the cognitive ability of patients with cognitive impairment, after collation and extraction of data from relevant manuscripts, a small number of studies showed conflicted findings. In Lam et al. (2018) published results that were the converse of these conclusions. They studied the effects of WBV combined with a routine activity program on lower limb strength, balance, and mobility in community-dwelling individuals with mild or moderate dementia (Lam et al., 2018). They also used the Cantonese Mini-Mental State Examination (CMMSE) scale to evaluate the effect of WBV on the cognitive performance of 54 elderly patients with mild to moderate dementia (40 of whom were women). No significant differences in CMMSE scores or changes in outcomes were identified post-training or at the 3-month follow-up. In addition, myasthenia may be an important risk factor for cognitive impairment, since a clear correlation was found between them (Liu et al., 2020). In a clinical randomized controlled study of tai chi and WBV therapy in the elderly published by Zhu (2016), 90 male patients with myasthenia were randomly divided into WBV, tai chi, and control groups (Yaqiong, 2016). The WBV group underwent 12–16 Hz WBV training for 8 weeks (1 min for each group, 5 groups per day, 5 days per week). An MMSE was used to evaluate the cognitive ability of subjects before and after the experiment. The results indicated no significant changes in cognitive ability in the three groups after the experiment. Thus, WBV training did not affect cognitive function in male patients with myasthenia. The results of that study were quite different from the results of other studies, possibly due to differences in amplitude, frequency, and training posture. Therefore, it has been suggested that an in-depth study of amplitude and other factors should be conducted. The differences may also be related to monitoring and evaluation indicators and methods. As science and technology continuously progress, methods of evaluation and studying cognitive function constantly improve. Future studies should combine a variety of methods that perform evaluation not only using scales of intelligence, language, memory, and attention but also using objective methods, such as EEG, functional magnetic resonance imaging, functional near-infrared spectroscopy, and transcranial Doppler ultrasound.

Discussion

The aim of this systematic review was to determine changes in cognitive ability after WBV training in healthy individuals and in patients with cognitive impairment. The key findings of the majority of studies included in this review were that WBV training had a positive effect on healthy individuals and those with cognitive impairment. Three studies produced contradictory results, thereby suggesting that WBV treatment had no significant effect on the cognitive ability of healthy individuals and patients with cognitive impairment. WBV training provides a potential cognitive rehabilitation technique for patients with weakness or balance defects. No systematic review has been performed comparing WBV training in cognitive improvement. The present systematic review is important because it analyzes WBV training as a potential aid to cognitive rehabilitation.

Until now, the underlying mechanisms of WBV training that improve cognition remained unclear. Literature review over the years has shown that the majority of studies support the following hypotheses: vibrations produced by WBV can stimulate skin mechanosensory receptors, such as tactile corpuscles, and these mechanoreceptor signals are transmitted to the primary somatosensory cortex. The areas that are associated have a direct and indirect connection with the prefrontal cortex, a region strongly involved in cognitive processing (Braak et al., 1996; Regterschot et al., 2014). The indirect pathways involve the limbic system (such as the amygdala and hippocampus, important areas of learning and memory), which can mediate the effects of sensory correlations on the prefrontal cortex (Durgut et al., 2020). Furthermore, the amygdala has projections to non-thalamic nuclei (e.g., the cholinergic nuclei of the basal forebrain) that have diffuse connections to several brain regions (Braak et al., 1996). Therefore, it has been speculated that this sensory stimulation can improve the cognitive function of the brain by affecting neural transmission of the prefrontal cortex and in regions around the inferior frontal sulcus by increasing the connectivity between neuronal dendrites. A number of studies have demonstrated that WBV training can change the neuromuscular recruitment pattern and muscle length, stimulate muscle spindles, and induce a stretch reflex response, which ultimately leads to stimulation of afferent neurons and irritability of the corticospinal pathways, with an increased oxygen uptake and heart rate (Amonette et al., 2015; Lam et al., 2018; Fereydounnia and Shadmehr, 2020). Changes in heart rate after WBV intervention not only depended on the sympathetic and parasympathetic balance but also directly correlated with the level of activity in the prefrontal cortex (Herrero et al., 2011). In addition, Kim and Lee (2018) performed EEG analysis and demonstrated that, after WBV training, alpha waves in the frontal lobe, which can activate the cerebral cortex, increased significantly, and are beneficial for cognition.

Furthermore, when data from the literature were collected and analyzed, it was found that WBV training could improve the cognitive ability of animals. In Keijser et al. (2017) described the relationship between WBV training and cognition in the mouse for the first time using a model of WBV in which attention and motor performance were improved. They randomly divided 44 male mice into a WBV and control group. The WBV group received 5 weeks of WBV training at 30 Hz and 1.9 g amplitude, 5 days a week for 5 or 30 min on each occasion, while the control group received sham vibration training. It was found that short-term WBV training improved the attention and motor performance of mice. Subsequently, Boerema et al. (2018) trained 10 mice at 30 Hz for 5 weeks (10 min per day, 5 days per week), then analyzed them with positron emission tomography. The results indicated that brain glucose uptake did not change, but motor performance improved (Boerema et al., 2018). Finally, combined with a selective improvement in the human Stroop Test, it was concluded that WBV is a safe intervention that improves brain function. However, the data showed that WBV training improved brain function, but specific improvements in brain function were not analyzed. In the same year, Raval et al. (2018) explored the effectiveness of WBV at reducing post-ischemic stroke and brain injury in reproductively senescent female rats. The animals were divided randomly into a WBV and non-WBV group (Raval et al., 2018). The WBV group was treated with WBV at 40 Hz for 30 days (15 min, twice per day, 5 days per week). Motor function and markers of brain inflammation were measured using histopathology, the results demonstrating that compared with the non-WBV group, inflammatory markers and the volume of the infarct decreased significantly, the level of brain-derived neurotrophic factor increased significantly, and functional activity improved significantly in the WBV group. The principal mechanisms by which WBV training activated/increased the cognitive ability of mice are as follows: (I) forebrain cholinergic system activity; (II) glucose transport across the blood-brain barrier; (III) immediate early gene expression (enhancing neuronal responsiveness); (IV) production of proteins required for neuronal plasticity; (V) production of new neurons; (VI) increased concentration of tyrosine hydroxylase, the enzyme responsible for the synthesis of the precursor of the neurotransmitter dopamine (Fuermaier et al., 2014a). Studies have shown that dopamine affects exercise, motivation, and cognition, and it has been confirmed that it is associated with the pathophysiology of ADHD (Fuermaier et al., 2014a).

Despite the positive findings reported in this systematic review, the discrepancies in the literature regarding the benefits of WBV training on cognitive ability require explanation. Improvements in cognition observed with WBV training may depend on a variety of factors that interact with one another, such as frequency, amplitude, and duration of intervention, possibly explaining the contradictory results. Based on the available data, analysis demonstrates that a beneficial frequency of vibration is from 12 to 50 Hz and an amplitude of 0.44 to 5 mm. Eight studies used a vibratory frequency of 30 Hz, but various amplitudes. This may be related to its mechanism of action. The study by Regterschot et al. (2014) suggests that mechanoreceptors in the skin, such as the Meissner corpuscles, are particularly sensitive to vibrations at 30–40 Hz. These differences make it difficult for parameters of an exercise program to be established, and it is not possible to draw a clear conclusion to determine the best parameters for WBV training. In addition, the methods and means of evaluating cognitive function are also important in qualifying the analysis of the research results. It is worth noting that of the 15 articles included in the study, the Stroop Test is the most frequently used method of evaluation of cognitive function. In addition, several studies chose EEG, reaction time, and MMSE to analyze the experimental results. Interestingly, in three articles, the MMSE scale was used to evaluate the effects of WBV training on cognitive function, while in two articles, it was considered that WBV training did not have a positive effect on cognitive function.

Limitations

The current review has several limitations that should be considered when interpreting the results. Firstly, only a small number of publications related to WBV and cognitive function were found. Secondly, the search strategy did not include a search for any unpublished literature in this area. Therefore, it is possible that relevant studies may have been missed. Thirdly, due to methodological differences in biomechanical parameters, the type of vibration, and variability in the duration of treatment, the conclusions of this review should be interpreted carefully. Finally, the populations included in these studies were heterogeneous due to differences in age and symptoms. In addition, the guidelines of van Heuvelen et al. (2021) are recommended to promote correct, complete, and consistent WBV reporting for future studies.

Conclusion

To summarize, WBV training is a method that stimulates and promotes the central nervous system by causing repeated contractions and relaxation in muscles through rapid vibration. Its application and related studies in the field of cognition are still considered novel. We have reviewed relevant studies of the role of this technology in cognitive function and found that WBV training has some contradictory effects on cognition and brain function, but the most studies suggest that WBV training positively influences cognitive performance. Although there are individual studies that suggest that WBV treatment does not significantly improve cognitive ability, it has been pointed out that WBV exercise does not negatively affect neuro-cognition. Therefore, WBV training should be considered for inclusion in rehabilitation programs, but further studies are required to strengthen the reported results. There has been no unified or standardized research design or method of intervention, possibly an important reason for differences in the conclusions of each study. We anticipate that this review will promote studies on the relationship between WBV and cognitive function, with further studies and exploration of the dose-effect relationship of WBV, physical parameters of vibration, the therapeutic effects on different subjects, and potential mechanisms of adaptive change in cognitive ability. Finally, this could result in the development of a scientifically based and effective WBV training system.

Data availability statement

The original contributions presented in this study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

JW, JH, and LL drafted the project plan and protocol. JW performed the literature search. JW and LL screened and evaluated the articles. JH and JW performed the statistical analysis. MH performed the evaluation of clinical relevance. MH and XH supported the analysis of WBV training during the screening process. All authors were involved in data interpretation, drafting of the manuscript, and revisions.

Funding

Financial support was received from the Humanities and Social Science Foundation of Ministry of Education of China (18YJC880035), the National Natural Science Foundation of China (31771315 and 31971105), the Open Fund of the Guangdong Provincial Key Laboratory of Physical Activity and Health Promotion (2021B1212040014), and the National Social Science Foundation of China (19BTY126).

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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