

Review

Look into my eyes: What can eye-based measures tell us about the relationship between physical activity and cognitive performance?

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Received 12 January 2023; revised 7 March 2023; accepted 16 March 2023

Available online 5 May 2023

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Abstract

Background: There is a growing interest to understand the neurobiological mechanisms that drive the positive associations of physical activity and fitness with measures of cognitive performance. To better understand those mechanisms, several studies have employed eye-based measures (e.g., eye movement measures such as saccades, pupillary measures such as pupil dilation, and vascular measures such as retinal vessel diameter) deemed to be proxies for specific neurobiological mechanisms. However, there is currently no systematic review providing a comprehensive overview of these studies in the field of exercise-cognition science. Thus, this review aimed to address that gap in the literature.

Methods: To identify eligible studies, we searched 5 electronic databases on October 23, 2022. Two researchers independently extracted data and assessed the risk of bias using a modified version of the Tool for the assessment of Study quality and reporting in EXercise (TESTEX scale, for interventional studies) and the critical appraisal tool from the Joanna Briggs Institute (for cross-sectional studies).

Results: Our systematic review ($n = 35$ studies) offers the following main findings: (a) there is insufficient evidence available to draw solid conclusions concerning gaze-fixation-based measures; (b) the evidence that pupillometric measures, which are a proxy for the noradrenergic system, can explain the positive effect of acute exercise and cardiorespiratory fitness on cognitive performance is mixed; (c) physical training- or fitness-related changes of the cerebrovascular system (operationalized via changes in retinal vasculature) are, in general, positively associated with cognitive performance improvements; (d) acute and chronic physical exercises show a positive effect based on an oculomotor-based measure of executive function

Peer review under responsibility of Shanghai University of Sport.

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<https://doi.org/10.1016/j.jshs.2023.04.003>

Cite this article: Zou L, Herold F, Ludyga S, et al. Look into my eyes: What can eye-based measures tell us about the relationship between physical activity and cognitive performance? *J Sport Health Sci* 2023;12:568–91.

(operationalized via antisaccade tasks); and (e) the positive association between cardiorespiratory fitness and cognitive performance is partly mediated by the dopaminergic system (operationalized via spontaneous eye-blink rate).

Conclusion: This systematic review offers confirmation that eye-based measures can provide valuable insight into the neurobiological mechanisms that may drive positive associations between physical activity and fitness and measures of cognitive performance. However, due to the limited number of studies utilizing specific methods for obtaining eye-based measures (e.g., pupillometry, retinal vessel analysis, spontaneous eye blink rate) or investigating a possible dose–response relationship, further research is necessary before more nuanced conclusions can be drawn. Given that eye-based measures are economical and non-invasive, we hope this review will foster the future application of eye-based measures in the field of exercise-cognition science.

Keywords: Cognition; Exercise; Fitness; Pupil size; Retina

1. Introduction

Accumulating evidence suggests that engagement in physical activity (including regular, planned, and structured forms such as acute and chronic physical exercise)¹ and the maintenance of a relatively high level of fitness in different dimensions (e.g., cardiorespiratory fitness, muscular strength, and motor fitness) can exert a positive effect on attentional control and higher-order cognitive functions (e.g., executive function and episodic memory) across different age groups and health conditions.^{2–9} However, a more detailed analysis of the literature also suggests that the positive effects are not universal as many studies did not observe, for instance, a significant effect of acute physical exercise on behavioral measures.¹⁰ Thus, a better understanding of the neurobiological mechanisms driving the positive effects of higher levels of physical activity (e.g., acute and chronic physical exercises) and fitness on cognitive performance is required.^{6,8,11–13}

To gain deeper insight into the neurobiological mechanisms that underlie exercise- and fitness-induced cognitive benefits, studies have applied different neuroimaging methods. For example, recent advances in neuroimaging technology (i.e., structural magnetic resonance imaging (MRI) and functional MRI (fMRI), functional near-infrared spectroscopy (fNIRS) and event-related optical signals, and electroencephalography (EEG)) have enabled researchers across different disciplines (e.g., exercise science, medicine, neuropsychology, and neuroscience) to deepen our understanding of the neurobiological changes contributing to the positive association of physical activity and different fitness dimensions with cognitive and brain health. With the number of cross-sectional and interventional studies increasing over the last 2 decades, there has also been an increase in the number of high-quality reviews conducted to evaluate the findings and application of these different neuroimaging techniques and to summarize the current state of the literature. These reviews have focused on neuroimaging techniques to either assess physical activity- and fitness-related changes in brain patterns using EEG,^{14,15} fNIRS,^{16,17} and fMRI^{18–21} or to evaluate changes in brain structure using MRI.^{20–22} These reviews have advanced our understanding of the neurobiological mechanisms that may underlie the enhanced cognitive performance observed following participation in certain forms of physical activity and that are associated with a higher fitness level across different fitness dimensions. However, the application of neuroimaging methods can be challenging (e.g., in terms of cost and preparation) and, at least for some participants (e.g., children with autism spectrum disorder), difficult, stressful, and uncomfortable because, for example, of the need to lie as motionless as possible in fMRI or

to wear an electrode cap and wash their hair after the experiment due to the use of electrode gel in EEG.^{16,23} Furthermore, the time needed to collect data via neuroimaging tools is relatively high (e.g., due to preparation). An overly reductionist approach (e.g., focusing only on neuroimaging) is insufficient to foster a comprehensive understanding of brain-behavior relationships (e.g., the influence of physical activity on cognitive performance) and thus, from a (holistic) pluralistic view, behavioral work (e.g., using eye-based measures) should remain an integral part of neuroscientific research.²⁴ Perhaps due to the above-mentioned challenges, there is a growing number of studies utilizing indirect measures of brain functioning, such as eye-based measures, to elucidate potential neurobiological mechanisms associated with the positive effects of physical activity and fitness on cognitive performance. As the potential of eye-based measures has begun to be recognized in exercise-cognition studies, this systematic review aims to provide a comprehensive overview of the current literature. Below, we briefly describe the eye-based measures and their links with different neurobiological mechanisms. Afterward, we outline some practical examples of how eye-based measures have been applied by researchers in the field.

1.1. Eye-based measures: A window into the neurobiological mechanisms that underlie the association of physical activity and physical fitness with cognitive performance

There is mounting evidence showing that tonic (i.e., obtained during resting state) and phasic (i.e., obtained during a cognitive task) eye-based measures can provide a unique window into the neurobiological processes that are relevant for cognition^{25–27} (see Fig. 1 for an overview). As there are many different eye-based metrics (e.g., measures based on oculomotor events such as fixations, saccades, or blinks or vascular measures such as retinal vessel diameters),^{28,29} a detailed description of all measures is beyond the scope of the current systematic review (for a detailed overview, please see Refs. 28 and 29). This review will focus on those eye-based measures associated with neurobiological mechanisms thought to underlie the positive association of physical activity and fitness with cognitive performance—namely, changes in neurotransmitters (e.g., catecholamines, such as dopamine and noradrenaline)^{5,30–32} or changes to the cerebrovascular system (as hypothesized in the cardiovascular/cardiorespiratory fitness hypothesis^{13,33–35} or cerebrovascular reserve hypothesis³⁶). Regarding the former point, selected measures of eye movement (i.e., pupil diameter, saccades, and spontaneous eye blink rate) related to the catecholaminergic system (in

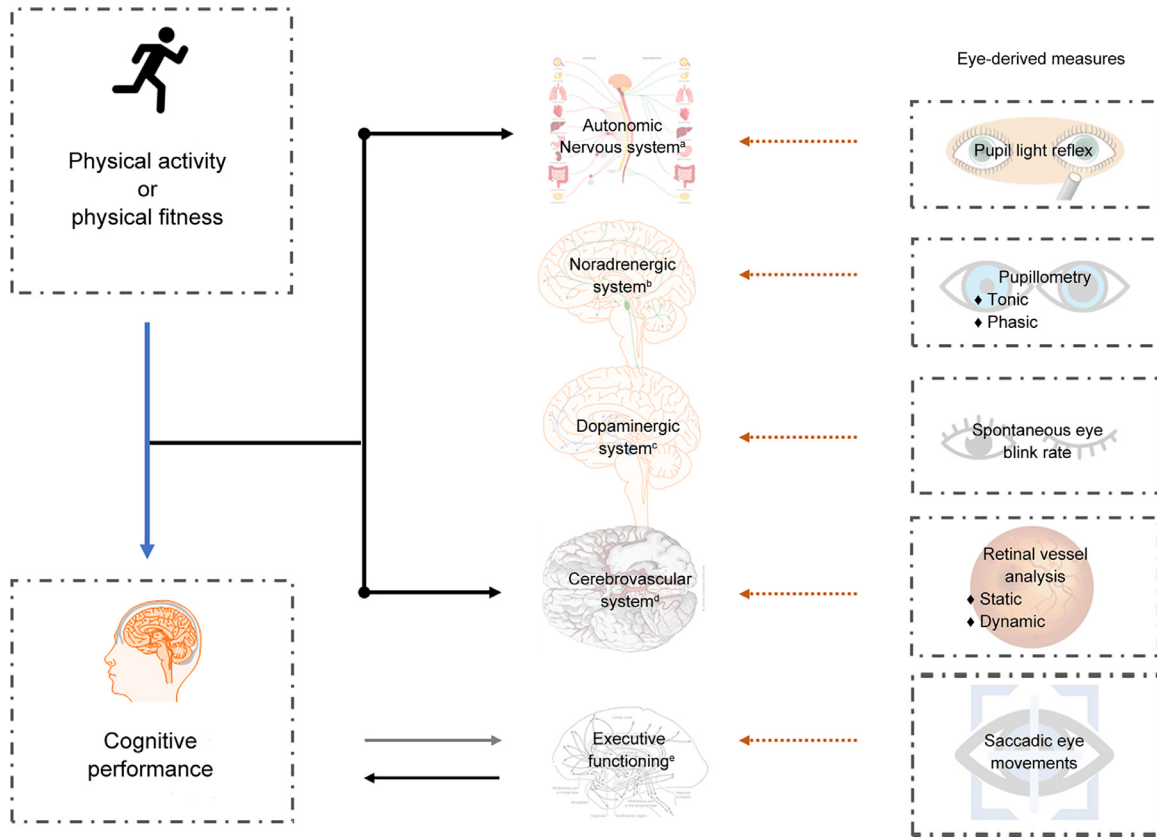


Fig. 1. Schematic overview of selected eye-based measures and their associations with distinct neurobiological mechanisms. ^aSuch as pupil light reflex.^{26,27} ^bBased on the findings of Refs. 5 and 27, although recent observations imply that pupil diameter is a result of a rather complex interplay of different neural systems²⁵ (e.g., the cholinergic system in the basal forebrain⁴⁷); ^c based on the findings of Refs. 73 and 96; ^d based on the findings of Ref. 60; ^e Based on the findings of Refs. 51 and 191.

particular, the noradrenergic system and the dopaminergic system) and selected measures of the retinal vasculature related to the cerebrovascular system are described below (Fig. 1):

- There is robust evidence indicating that pupillometry offers a readily and economically quantifiable, and non-invasive readout of the neural substrates of arousal and cognitive performance.^{25,26} In this context, pupil size has been linked to arousal-related changes to the activity of the noradrenergic system (i.e., locus coeruleus) in humans^{37–41} and animals,^{42–44} although the latter finding is not universal, and other studies suggest that changes in pupil size are linked to a more complex system (e.g., the cholinergic system in the basal forebrain).^{45–47} Nonetheless, as pupillometric changes at least to a certain extent reflect neurobiological processes that are important for cognitive performance (e.g., changes in noradrenergic system),^{25,26,48} pupil-size-based measures are frequently utilized in studies investigating cognitive performance (e.g., cognitive control, memory, decision making, language^{48,49}).
- Saccadic eye movements during standardized task conditions have been investigated widely in the fields of psychology, psychiatry, and neuroscience.^{49–52} In this context, prosaccade (i.e., saccade to the same direction as the visual stimulus) and antisaccade (i.e., saccade to the opposite direction as the visual stimulus) tasks are commonly utilized to study the saccadic control in different populations and conditions.^{49–52}

It is well-documented in the literature that saccadic movements are controlled by a complex network of subcortical and cortical neural structures.^{51–53} In particular, for human subjects to rotate and reorient their eyes, and thus to perform saccadic eye movements, they need to activate 3 pairs of extraocular muscles innervated by motor neurons of the cranial nerve nuclei;⁵⁴ meanwhile, antisaccade movements require the involvement of cortical neural structures (e.g., the prefrontal cortex), which are linked to higher-level cognitive processes, such as executive functioning.^{54,55}

- It is well-established in the literature that the dopaminergic system (e.g., frontostriatal circuit) is crucial for well-functioning cognitive performance.^{56–59} Regarding eye-based measures, there is some evidence that spontaneous eye-blink rate can be utilized as a proxy for the status of the dopaminergic system,⁶⁰ although this finding is not universal as some previous human studies reported no correlation to neuroimaging markers of the dopaminergic system (i.e., dopamine D2 receptor availability, striatal dopamine synthesis capacity).^{61,62} However, numerous studies have observed a link between tonic (resting state) spontaneous eye blink rate and cognitive performance^{63–65} or cognitive status⁶⁶ and phasic spontaneous eye blink rate (i.e., acquired during cognitive testing) and cognitive performance.^{67,68} Thus, it seems reasonable to assume that spontaneous eye blink rate reflects specific brain processes (e.g., activation of the dopaminergic

system). This assumption is supported by evidence suggesting a relationship between tonic spontaneous eye blink rate and (a) theta power in typically and atypically developing children,⁶⁹ (b) N2 amplitudes of the stimulus-locked event-related brain potential under Go- and No-Go-conditions⁷⁰ or only a No-Go condition in younger healthy adults,⁷¹ and (c) activity of the angular gyrus in younger healthy adults.⁷²

- Vascular eye-based measures are considered a proxy for the status of the cerebrovascular system,^{73,74} which is assumed to play, among other factors, a vital role in the positive relationship between physical activity and fitness and measures of cognitive performance.^{13,34,36,75} Various approaches can be used to assess the retinal vasculature, such as optical coherence tomography angiography^{76–78} or static and dynamic retinal vessel analysis.²⁹ For a more detailed description of the methods please see Refs. 29,76–78.

As outlined above, eye-based measures can provide a unique window into the neurobiological processes relevant to cognition and, perhaps, those that drive the positive association between physical activity and fitness and measures of cognitive performance. Eye-based measures provide several advantages:

- Specific eye-based measures are a non-invasive proxy that at least partly mirror neurobiological mechanisms whose direct assessment is relatively difficult and rather expensive (e.g., changes in the noradrenergic or dopaminergic system;^{25,26,60} Fig. 1). Thus, specific eye-based measures might constitute an accessible and economical alternative to invasive, expensive, and more complex neuroimaging methods (e.g., positron emission tomography to assess the activity of the dopaminergic system), which often cannot be repeated within short periods of time (e.g., in an acute physical exercise study using a within-subject crossover design with pretest/post-test comparison).⁵ Moreover, eye-based measures such as the pupil light reflex are considered a proxy for the state of the autonomic nervous system^{26,27} and, as such, might complement more traditional measures of the autonomic nervous system (e.g., heart rate variability^{79–81}) already used in the field of exercise-cognition science (e.g., Refs. 82 and 83). In this context, eye-based metrics may constitute a useful complement to other invasive (e.g., blood samplings to assess, for instance, the concentration of the brain-derived neurotrophic factor)^{84,85} and non-invasive measures (e.g., saliva assessments to determine testosterone levels)^{86,87} currently being used to comprehend the neurobiological processes behind the positive effects of physical activity and/or fitness on cognitive performance.
- Eye-based measures are easily assessed in combination with other non-invasive neuroimaging modalities (e.g., EEG and/or fNIRS).^{88,89} Taking an approach that simultaneously considers multiple levels of analysis may allow for a more comprehensive understanding of the relative contribution of distinct neurobiological mechanisms.^{6,8,11} Researchers might seek to determine, for example, how an acute exercise-induced change in a neuro-modulatory system (e.g., noradrenergic or dopaminergic) will influence cortical brain activation during a cognitive test.

- Eye-based measures (e.g., saccadic eye movements) are typically hand- and language-free measures, which can help circumvent some of the challenges associated with typical neuropsychological-based measures. That is, they allow cognitive testing in cohorts with language or motor impairments.^{90,91}

The advantages of eye-based measures highlight their promise for the field of exercise-cognition science. Next we explore some practical applications of eye-based measures to see how they have been used to better understand the positive influence of physical activity and fitness on cognitive performance.

1.2. Practical applications of eye-based measures in the field of exercise–cognition science

Recent works^{92,93} have demonstrated better cognitive performance and increased tonic pupil dilation (i.e., at rest) during inhibitory control tasks following acute bouts of physical exercise in samples of younger adults ($n = 16$ ⁹² and $n = 43$ ⁹³). While these findings suggest an exercise-induced increase in the arousal-related activation of the locus-coeruleus norepinephrine system (operationalized by tonic pupil dilation), there is no evidence for a correlation between changes in tonic pupil dilation and exercise-induced change in cognitive performance.⁹³ A cross-sectional study in younger adults ($n = 126$)⁹⁴ did not find evidence that phasic pupil dilation (which was obtained during a Flanker task and is a marker of activation of the locus-coeruleus norepinephrine system) mediates the positive relationship between higher cardiorespiratory fitness and shorter reaction time in an inhibitory control task. Findings from another cross-sectional study using resting-state spontaneous eye blink rate—an indirect marker of the activity of the dopaminergic system⁶⁰—suggested that in younger male adults ($n = 35$) resting-state spontaneous eye blink rate mediates the relationship between cardiorespiratory fitness level and cognitive performance.⁹⁵

Vascular eye-based measures, such as the diameter of retinal arteries and veins assessed via static retinal vessel analysis, reveal important information about the cerebrovascular system.^{73,96} A cross-sectional study in primary school children ($n = 347$) showed that markers of retinal microcirculation explained a unique portion of the variance in cognitive performance (i.e., inhibitory control and information processing) in children even after accounting for traditional markers of cardiovascular disease risk (i.e., body mass index, systolic and diastolic blood pressure).⁹⁷ With respect to physical activity, a randomized controlled trial investigating the effects of an 8-week aerobic and coordinative training intervention in adolescents ($n = 35$) reported that changes in retinal arteriolar diameter were positively correlated with changes in cognitive performance (i.e., shorter reaction time during an inhibitory control task).⁹⁶ This latter finding suggests that vascular eye-based measures might constitute a new approach to understanding the influence of physical activity on select neurobiological systems.

Taken together, these few examples are not exhaustive, but they illustrate the potential for eye-based measures to help researchers clarify the roles of distinct neurobiological mechanisms that drive the positive effects of physical activity and fitness on cognitive performance.

1.3. Objective of this systematic review

The evidence presented above corroborates the value of eye-based measures as an investigative tool. The visual system is especially crucial for the kinds of cognitive tests that are frequently used in the field of exercise-cognition science (e.g., Stroop, n-back, or Flanker tasks).⁵ However, despite the initially promising findings of eye-based measures and their associations with physical activity, physical fitness, and cognitive performance, there has been no systematic review of available studies to date. By presenting the current state of knowledge on the application of eye-based measures in the field of exercise-cognition (e.g., methodological information including state-of-the-art data processing recommendations), a systematic and methodologically focused review would serve as a valuable resource for scholars across research fields such as exercise science, medicine, neuropsychology, and neuroscience. Thus, our systematic review addresses the gap in the literature by providing a comprehensive survey of the application of eye-based measures in the field of exercise-cognition science with a specific focus on methodological details (see [Supplementary materials](#); Method section). We performed an analysis of the potential influence of exercise and training characteristics as there is evidence to suggest the type of physical activity (e.g., endurance, resistance, or coordinative exercise),^{2,7,98} as well as exercise intensity⁴ and frequency,⁹⁹ may differentially influence measures of cognitive performance and neuroimaging.

2. Methods

This systematic review was conducted in line with established guidelines^{100–103} and was preregistered in the Open Science Framework (registration at: <https://osf.io/cgz8x/>).

2.1. Search strategy

As recommended by established guidelines,^{100–103} the literature search for this systematic review was conducted by 2 independent researchers (FH and LZ) on October 23, 2022. Five electronic databases (applied filters) were searched from inception to October 23, 2022: PubMed (all fields), Scopus (title/abstract), Web of Science (title), PsycInfo (all text), and SPORTDiscus (all text). Thereto, a specific search string was developed (see [Supplementary materials](#) for more details), and the results of the systematic literature search were stored as supplementary materials in the Open Science Framework account (<https://osf.io/cgz8x/>) managed by LZ.

2.2. Inclusion and exclusion criteria

In accordance with established guidelines,^{100,101} the current systematic review defined inclusion and exclusion criteria based on the PICOS-principle: Participants, Intervention, Comparison, Outcomes, and Study design.

- Participants: Studies with human participants, regardless of age and health status, were included.
- Intervention: With respect to interventional studies, we included those that investigated the effects of a single bout of physical exercise (i.e., acute physical exercise) or of

chronic physical exercise (e.g., physical training, such as resistance training or aerobic exercise training).

- Comparison: Concerning cross-sectional studies, those that investigated the effects of physical activity, different fitness domains (i.e., cardiorespiratory, muscular, and motor fitness), or a related variable on eye-based measures and cognitive performance were included. In terms of interventional studies, all those that investigated the influence of physical exercise interventions on eye-based measures and cognitive performance were included, regardless of whether or not a non-exercise control group was utilized (i.e., feasibility or pilot studies) and regardless of type of physical exercise. In this context, *active* refers to a condition that involves the execution of the physical activity, whereas *passive* refers to a condition in which the participants were typically asked to take a seated rest (e.g., reading) for the duration of the acute intervention (i.e., in acute physical exercise studies) or to maintain their level of regular physical activity (i.e., in chronic physical exercise studies).
- Outcome(s): We included all studies that assessed, at minimum, 1 outcome within the 3 following categories: (a) an eye-based measure, (b) a measure of cognitive performance, and (c) a measure of physical activity or physical fitness.
- Study design: This systematic review included both cross-sectional and interventional studies (e.g., single-group pre-to-post design, non-randomized controlled trials, or randomized cross-over controlled trials). Review articles, posters, study protocols, and studies written in a language other than English were excluded.

All studies that did not meet the above-mentioned inclusion criteria for participants, comparison, outcome(s), and study design were excluded. Furthermore, as we conducted our systematic review on October 23, 2022, studies published after this date were not included.

2.3. Screening

Following the electronic database search, 2 researchers (FH and LZ) independently screened the retrieved results using a 3-step process. In the first step, duplicates were removed by the reference managing software (Endnote 20; Clarivate, Philadelphia, PA, USA). In the second step, the title and abstract were evaluated against eligibility criteria. If the researchers were unable to reach a decision regarding eligibility solely based on the information provided by title and abstract, a third step was taken to conduct a screening of the full text. In cases where there was disagreement between the researchers concerning the eligibility of a study, a third reviewer (SL) was consulted to reach a final decision. The search, screening, and selection processes that led to the identification of relevant articles are shown in [Fig. 2](#) and described in more detail in [Section 3.1](#).

2.4. Data extraction

The data extraction procedures in the current systematic review replicate those used in other systemic and methodology-focused reviews in the field of exercise science.^{16,18,104}

Thus, we extracted the following data from cross-sectional and interventional studies.

- Population characteristics (e.g., age, gender, health status, and fitness level).
- Intervention-related characteristics (e.g., exercise intensity, duration, and type of exercise).
- Cognitive testing (e.g., tested cognitive domain, administration after exercise cessation or after acute exercise bouts).
- Methodological information (e.g., data processing procedures and data analysis).
- Main findings ((non)-significant difference, (non)-significant association, and/or (non)-significant indirect effect/mediation).

The data extraction was performed by 2 independent researchers (FH and LZ) using a standardized procedure. Specifically, each researcher independently extracted data from half of the relevant studies. Afterward, each reviewer checked the data extraction of the other. If any discrepancies were found, a third reviewer (SL) was consulted to reach

consensus. In cases where the 2 researchers were unable to identify and extract some specific data or piece of information from the original article, they (or another co-author) contacted the original investigator at least 3 times via e-mail or social networks (i.e., ResearchGate) to request further information.

2.5. Risk of bias assessment

Two independent researchers (FH and LZ) conducted the risk of bias assessment using a modified version of the Tool for the assessment of Study quality and reporting in EXercise (TESTEX scale)¹⁰⁵ for interventional studies and the critical appraisal tool from the Joanna Briggs Institute for cross-sectional studies.¹⁰⁶ Regarding interventional studies, the TESTEX scale evaluates the methodological quality of every study by rating the risk of bias for distinct criteria;¹⁰⁵ and in our modified version of the TESTEX scale, we rated the risk of bias as “low”, “high”, or “unclear” (see [Supplementary materials](#) for further details). We intentionally refrained from calculating a summary score given the disadvantages of such an approach (for discussion see Ref. 107). Regarding cross-sectional studies, the Joanna Briggs Institute critical appraisal

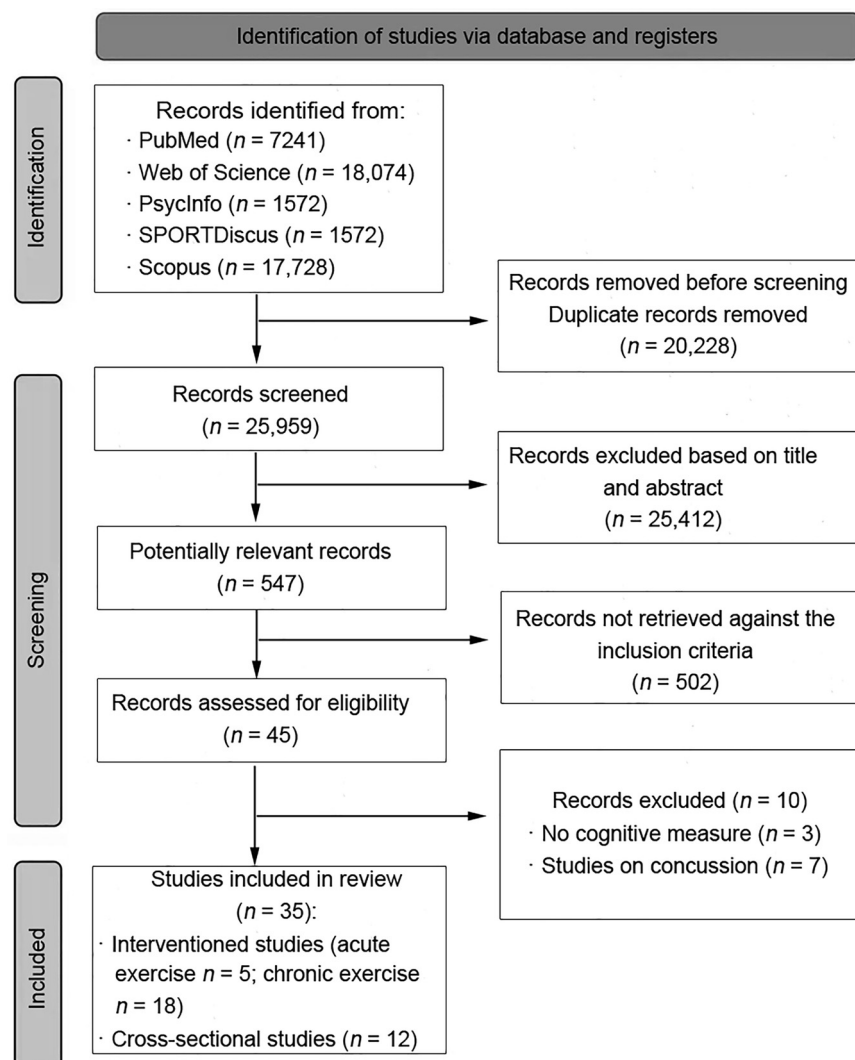


Fig. 2. Flow diagram of data search, screening, and assessment.

tool was used to assess bias by rating the methodological quality of each study according to a standardized set of questions answered as: “Yes”, “No”, “Unclear”, or “Not/Applicable”.¹⁰⁷ If any discrepancies in the risk of bias ratings occurred between the 2 researchers (LZ and FH), these were resolved by discussion in consultation with the third author (SL).

3. Results

3.1. Study selection

As shown in Fig. 2, a total of 46,187 records were initially identified in the 5 databases. Nearly 43.8% of them ($n = 20,228$) were duplicates and were removed. The remainder were screened by title and abstract, yielding 547 potentially relevant records. These were then examined in detail against the inclusion and exclusion criteria, and 45 full-text records were selected for final assessment. Ten studies that either did not include a cognitive measure ($n = 3$) or that focused on concussion ($n = 7$) were removed. The final sample included 35 relevant studies for analysis in this systematic review.

3.2. Study characteristics

As shown in Table 1, the majority of included studies were conducted in Western countries, such as Canada and the United States, and were published in the previous 5 years, indicating a rapidly growing research interest. Of note, 12 of the 35 studies used cross-sectional designs that investigated associations between regular physical activity, physical fitness, cognitive performance, and eye-based measures.^{94,95,108–117} Five trials studied the effect of chronic physical training on cognitive performance and eye-based measures,^{96,118–121} and 18 studies investigated the influence of an acute bout of physical exercise on cognitive performance and eye-based measures.^{92,93,122–137}

Most of the reviewed studies included younger healthy adults with normal cognitive performance (based on the inclusion and exclusion criteria of the respective studies) who were mainly students and could be classified as recreationally active,^{92–95,108,111,122–124,126–132,135,137} whereas 6 of the studies compared different types of younger athletes.^{109,110,114–116,136} The remaining trials examined (a) healthy school-aged children,⁹⁶ (b) younger adults with mobile phone addiction,¹³⁴ (c) healthy community-dwelling older adults,^{119,125,133} (d) older adults with self-reported cognitive complaints¹¹⁸ and type 2 diabetes mellitus,¹²¹ (e) older adults with objective cognitive impairments,¹¹⁹ (f) healthy older adults,^{113,120} or (g) a population with a broad age range from 18 to 60 years¹¹² (Table 1).

3.3. Exercise and training characteristics

All acute physical exercise studies investigated the effects of continuous endurance exercise (either conducted on a treadmill^{93,125,132,135,137} or stationary cycling ergometer^{92,122–124,126–131,133,134}). One study conducted an intermittent (interval) exercise protocol on a stationary cycle ergometer¹³³ while another had participants engage in high-intensity interval boxing exercises.¹³⁶ In 13 studies, the exercise intensity was set using a specific percentage of maximal

heart rate^{92,93,118,119,124,126,128,129,132,134,136} or heart rate reserve.^{133,135} The maximal heart rate was predicted using specific formulas (i.e., $(205.8 - (0.685 \times \text{age}))$,¹³² $(207 - (0.7 \times \text{age}))$,¹³⁶ $(220 - \text{age in years})$ ^{92,124,126,128,129,134}), or determined using maximal values obtained during a graded exercise test⁹³ or step test.^{118,119} A detailed overview of exercise intensity and exercise duration for included studies is provided in Table 1. In addition, the settings of the reviewed acute physical exercise studies can be classified as individual and laboratory-based^{92,93,122–132,134,135} or gym-based.¹³⁶

With respect to the studies investigating the influence of chronic physical training on cognitive performance and eye-based measures, the following interventions were conducted: (a) a combination of aerobic and coordinative exercises,⁹⁶ (b) multimodal exercises (including aerobic, resistance, balance, and breathing or stepping exercises),¹¹⁸ (c) a combination of cognitive-motor and aerobic exercises,¹¹⁹ (d) high-speed circuit resistance training,¹²⁰ (e) square stepping exercises,¹²¹ and (f) individual preparation for a marathon.¹¹² The interventions lasted 8 weeks^{96,120} or 24 weeks.^{118,119,121} The training sessions ranged from 2 sessions per week on non-consecutive days,¹²¹ 3 sessions per week¹²⁰ or 3 sessions per week on non-consecutive days (i.e., Monday, Wednesday, and Friday),^{118,119} to 5 sessions per week on consecutive days (i.e., all weekdays).⁹⁶ In these chronic exercise intervention studies, participants completed an individual¹¹⁹ or group-based physical training program.^{96,118,121} The completion adherence, defined as the absolute number of individuals still attending the class at follow-up in relation to the number of individuals enrolled at the start of the intervention,^{138,139} was as follows: $\sim 100\%$,¹¹⁸ 95% ,⁹⁶ 88.4% ,¹¹⁹ and $\sim 67\%$.¹²¹ Attendance adherence, defined as the actual and visited number of training sessions in relation to the total number of offered/recommended training sessions,^{138,139} was as follows: $\sim 87\%$,¹¹⁹ $\sim 79\%$,⁹⁶ 77% , and 72% (for the 2 intervention groups, respectively),¹¹⁸ and $> 50\%$ for 70.2% of the participants.¹²¹ In 3 of the studies, no intervention-related adverse events occurred,^{96,118,119} whereas a minor event (i.e., headache) occurred in 1 study.¹²¹ In another study, researchers looked at the chronic effects of marathon preparation and the acute effects of running a marathon, but because all participants performed their own marathon preparation program, no specific exercise or training-related characteristics were reported.¹¹²

3.4. Main findings

3.4.1. Fixation

A cross-sectional study reported that the odds of gazing first at and gaze duration on a physically active (vs. physically inactive) stimulus increased with higher levels of physical activity.¹¹⁷ However, a study investigating the effects of an acute bout of physical exercise on fixation parameters during a facial emotion task did not observe such an exercise-induced effect on fixation duration, longest fixation, number of fixations, or scan path length.¹³⁵

3.4.2. Pupillometry

In 2 of the reviewed studies, phasic pupil size was positively associated with a higher level of cardiorespiratory fitness,^{93,108} whereas tonic pupil size was positively associated

Table 1

Overview of study characteristics (i.e., study design and sample characteristics, characteristics of the physical intervention, and cognitive measures and main findings).

Study	Study design and sample characteristics	Characteristics of the physical interventions	Cognitive testing and main findings
	(1) Study design (2) Comparison group/condition (3) Participants' characteristics ■ Mean age $\pm$ SD (3.1) Cardiorespiratory fitness level/Level of regular physical activity (3.2) Mean body height $\pm$ SD/Mean body mass $\pm$ SD/BMI $\pm$ SD ■ PIA: 21.6 ± 3.2 years (3.1) PA: 378.0 ± 310.0 min/week; PIA: 57.0 ± 47.0 min/week (3.2) n.a./n.a./PA: 21.8 ± 3.8 kg/m ² ; PIA: 21.3 ± 2.5 kg/m ²	(1) Exercise intensity (2) Duration of an exercise session	Main findings related to cognition and eye-derived measures
Fixation			
Cheval et al. (2020) ¹¹⁷	(1) Cross-sectional study (2) PA vs. PIA (3) Healthy young adults (students) ■ PA: $n = 34$ (23 females/11 males) ■ PIA: $n = 43$ (29 females/14 males) ■ PA: 21.9 ± 3.0 years ■ PIA: 21.6 ± 3.2 years (3.1) PA: 378.0 ± 310.0 min/week; PIA: 57.0 ± 47.0 min/week (3.2) n.a./n.a./PA: 21.8 ± 3.8 kg/m ² ; PIA: 21.3 ± 2.5 kg/m ²	(1) n.a. (2) n.a.	(1) Visual dot-probe task (2) ■ ↓ RT in detecting a dot appearing in an area previously occupied by a physical activity (vs. inactivity) stimulus with the level of usual physical activity ■ ↑ odds of gazing first at and gaze duration on a physical activity (vs. inactivity) stimuli increased with a higher level of usual physical activity
Thom et al. (2021) ¹³⁵	(1) Non-randomized trial with within-subject cross-over design and pretest/post-test comparisons (2) Passive CG (i.e., seated rest) (3) Healthy younger adults ■ $n = 34$ (18 females) ■ 21.1 ± 1.4 years (3.1) 317.2 ± 44.3 kcals/week (3.2) n.a./n.a./ 23.3 ± 2.3 kg/m ²	(1) Vigorous intensity (65%–85% HRR) (2) 30 min	(1) Facial emotion task (2) ■ (–) No statistically significant differences between conditions concerning fixation measures
Pupillometry			
Ayala et al. (2021) ⁹²	(1) Non-randomized trial with pretest/post-test comparisons (2) n.a. (3) Healthy younger adults (students) ■ $n = 16$ (8 females/8 males) ■ 22.9 ± 1.9 years (3.1) Recreationally active based on GLTEQ (63 ± 16 points) (3.2) n.r./n.r. /n.r.	(1) Vigorous intensity (80% of predicted HR _{max}) and very light intensity in the warm-up and cool-down (50% of predicted HR _{max}) (2) 20 min (+ 2.5 min warm-up and cool-down, respectively)	(1) Pro- and antisaccade task (2) ■ ↓ Tonic pupil size and ↑ Phasic pupil size in pro- and antisaccade tasks from pretest to post-test
Cheval et al. (2020) ¹¹⁷	(1) Cross-sectional study (2) PA vs. PIA (3) Healthy young adults (students) ■ PA: $n = 34$ (23 females/11 males) ■ PIA: $n = 43$ (29 females/14 males) ■ PA: 21.9 ± 3.0 years ■ PIA: 21.6 ± 3.2 years (3.1) PA: 378.0 ± 310.0 min/week; PIA: 57.0 ± 47.0 min/week (3.2) n.a./n.a./PA: 21.8 ± 3.8 kg/m ² ; PIA: 21.3 ± 2.5 kg/m ²	(1) n.a. (2) n.a.	(1) Visual dot-probe task (2) ■ ↓ Phasic pupil size when participants with higher levels of regular physical activity viewed physically active (vs. inactive) stimuli
Chandler et al. (2021) ⁹⁴	(1) Cross-sectional study (2) Influence of CRF (3) Healthy younger adults (students) ■ $n = 126$ (100 females/26 males) ■ 19.1 ± 1.1 years	(1) n.a. (2) n.a.	(1) Modified Flanker task (2) ■ ↓ Negative correlation between RT and CRF ■ (–) Phasic pupil size did not mediate the positive correlation between reaction time

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Table 1 (Continued)

Study	Study design and sample characteristics	Characteristics of the physical interventions	Cognitive testing and main findings
McGowan et al. (2019) ¹³²	(3.1) 42.3 ± 9.0 mL/kg/min (3.2) n.r./n.r./n.r. (1) RCT with within-subject cross-over design and pretest/post-test comparisons (2) Active CC (3) Healthy younger adults (students) ■ $n = 58$ (32 females/26 males) ■ 19.2 ± 1.0 years (3.1) VO_{2peak} : 46.5 ± 8.7 mL/kg/min (3.2) n.a./n.a./ 24.6 ± 7.7 kg/m ²	(1) Moderate intensity (65%–75% of predicted HR_{max}) in EX/walking at 0.5 mph in active CC (2) 20 min	and CRF (adjusted for age, sex, race, body fat, and task congruency) (1) Modified Flanker task (2) ■ ↓ RT from pretest to post-test in EX ■ (–) Tonic pupil size and ↑ phasic pupil size from pretest to post-test ■ (–) Tonic pupil size and (–) phasic pupil size EX vs. CC ■ (–) No statistically significant correlations with exercise-induced changes in RT response accuracy P3 amplitude or P3 latency
McGowan et al. (2021) ¹⁰⁸	(1) Cross-sectional study (2) Influence of CRF (3) Healthy younger adults (college students) ■ $n = 137$ (74 females/63 males) ■ 18.9 ± 1.0 years (3.1) 44.8 ± 10.2 mL/kg/min (3.2) 171.6 ± 9.2 cm/ 71.9 ± 14.8 kg/ 24.3 ± 3.8 kg/m ²	(1) n.a. (2) n.a.	(1) Complex arithmetic task (2) ■ ↓ Negative correlation between RT and CRF ■ ↑ Phasic pupil size in difficult task conditions (i.e., small and large split) is positively associated with CRF (adjusted for age and sex)
Shigeta et al. (2021) ⁹³	(1) RCT with within-subject cross-over design and post-test comparisons (2) Passive CC (i.e., seated rest) (3) Healthy younger adults (college students) ■ $n = 38$ (21 females/17 males) ■ 19.7 ± 1.5 years (3.1) 52.4 ± 32.9 (fitness percentile) (3.2) n.a./n.a./ 23.8 ± 4.6 kg/m ²	(1) Light-to-moderate intensity (60%–70% HR_{max} measured during GXT) (2) 20 min (+ 1 min cool-down)	(1) Modified Flanker task (2) ■ ↓ RT in EX vs. CC ■ ↑ Tonic pupil size EX vs. CC ■ ↑ Low and positive correlation between phasic pupil size and CRF (i.e., across congruency conditions in EX)
Zhou et al. (2023) ¹¹¹	(1) Cross-sectional study (2) PA vs. PIA (3) Healthy younger adults ■ $n = 41$ (20 females/21 males) PA: $n = 26$ (11 females/15 males)/PIA: $n = 15$ (9 females/6 males) ■ 21.15 ± 1.15 years (3.1) PA: 5119.23 ± 1489.16 min/week; PIA: 153.60 ± 59.24 min/week (3.2) n.a./n.a./PA: 21.49 ± 1.66 kg/m ² ; PIA: 21.58 ± 1.44 kg/m ²	(1) n.a. (2) n.a.	(1) Antisaccade task (2) ■ ↓ SL and directional errors in PA vs. PIA ■ ↑ Tonic pupil size in PA vs. PIA ■ ↑ Low and positive correlation between the regular level of physical activity and pupil size
Retinal vessel analysis			
Fang et al. (2020) ¹²⁰	(1) RCT with between-subject design and pretest/post-test comparisons (2) Passive CG (i.e., no intervention) (3) Healthy older adults ■ EX: $n = 12$ (7 females/5 males) ■ CON: $n = 8$ (4 females/4 males) ■ EX: 70.8 ± 5.8 years ■ CON: 71.8 ± 4.8 years (3.1) n.r. (3.2) n.r.	(1) Light-to-moderate intensity (40%–65% of 1RM) (2) 40–45 min	(1) Mini-Mental State Examination and the NIH Toolbox Cognitive Battery (i.e., Flanker task, Dimensional Card Sort, Picture Sequence Memory Test, List Sorting Working Memory Test, and Pattern Comparison Processing Speed Test) (2) ■ ↑ Pattern Comparison Processing Speed Test (PAT) and Fluid Cognition Composite Score in EX (post- vs. pretest) ■ ↓ Moderate and negative correlation between changes in retinal vessel density of superficial vascular plexus and Fluid Cognition Composite Score and List Sorting Working Memory Test in EX
Fang et al. (2021) ¹¹³	(1) Cross-sectional study (2) Influence of CRF (3) Healthy older adults ■ $n = 20$ (11 females/9 males) ■ 71.2 ± 5.3 years (3.1) 16.6 ± 9.2 kJ (TW-YMCA) (3.2) n.a./n.a./ 29.0 ± 6.3 kg/m ²	(1) n.a. (2) n.a.	(1) Mini-Mental State Examination and Montreal Cognitive Assessment (2) ■ ↑ Moderately high and positive correlation between Montreal Cognitive Assessment score and vessel density of the retinal vascular network and superficial vascular plexus (adjusted for age, sex, education, and BMI)

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Table 1 (Continued)

Study	Study design and sample characteristics	Characteristics of the physical interventions	Cognitive testing and main findings
Ludyga et al. (2019) ⁹⁶	(1) RCT with between-subject design and pretest/post-test comparisons (2) Active CG (i.e., social interaction group) (3) Adolescents (pupils at private schools) ■ $n = 35$ (13 females/22 males) ■ 12.5 ± 0.2 years (3.1) MVPA: 119.1 ± 37.7 min/day (3.2) 154.8 ± 1.7 cm/n.a./ 18.2 ± 0.5 kg/m ²	(1) Moderate intensity (134.6 ± 9.4 beats/min) (2) 20 min	(1) Modified Stroop task (2) ■ ↓ RT in incongruent condition EX vs. CG at post-test ■ ↑ CRAE EX vs. CG at post-test ■ ↓ Moderate and negative correlation between change score (post–pre) of RT (i.e., incongruent trials) and CRAE (adjusted for sex and age)
Roeh et al. (2021) ¹¹²	(1) Cross-sectional study and non-randomized trial in EX (2) Passive CG (i.e., sedentary controls) (3) Healthy adults ■ EX: $n = 100$ (20 females/80 males) ■ CG: $n = 46$ (11 females/35 males) ■ EX: 43.6 ± 10.0 years ■ CG: 40.8 ± 11.0 years (3.1) EX: 46.5 ± 6.6 mL/kg/min EX: 7410.2 ± 7450.4 IPAQ score; CON: 3378.1 ± 6526.7 IPAQ score (3.2) n.a./n.a./EX: 23.5 ± 2.7 kg/m ² ; CG: 24.8 ± 2.7 kg/m ²	(1) individual (2) individual	(1) D2 test of attention, N-Back task, Trail Making Test A&B (2) ■ ↑ Positive correlation between discriminability index in the 3-Back task and AVR (adjusted for age and systolic blood pressure; chronic effect) ■ ↓ Negative correlation between discriminability index in the 3-Back task and CRVE (adjusted for age and systolic blood pressure; chronic effect ^a) ■ ↓ Negative correlation between time to complete TMT B and CRAE (adjusted for age and systolic blood pressure; chronic effect ^a) ■ ↑ Positive correlation between d2 concentration performance and CRAE (adjusted for age and systolic blood pressure; acute effect ^b) ■ ↓ Negative correlation between discriminability index in 1-Back task and time to complete TMT A with CRVE (adjusted for age and systolic blood pressure; acute effect ^b)
Solianik et al. (2021) ¹³⁶	(1) RCT with within-subject cross-over design and pretest/post-test comparisons (2) Passive CC (i.e. seated rest) (3) Healthy younger adults (boxer) ■ $n = 11$ (11 males) ■ 22.8 ± 2.9 years (3.1) 10.7 ± 4.8 years of boxing experience/Backe physical activity questionnaire score (work: 2.75 ± 0.70 , sport: 4.11 ± 0.41 , leisure: 5.75 ± 0.96) (3.2) 185.7 ± 8.6 cm/ 84.9 ± 13.1 kg/ 24.5 kg/m ²	(1) Vigorous intensity (~91% of predicted HR _{max}) (2) 21 min (including 10-min warm-up)	(1) Automated Neuropsychological Assessment Metrics test battery, including simple reaction time test, procedural reaction time test, mathematical processing test, and go/no-go test (2) ■ ↓ RT in procedural reaction time test and go/no-go test in EX (post- vs. pretest) ■ ↑ diameter of temporal retinal arterial venules (superior and inferior branch) for post- vs. pretest and compared to CC at post-test ■ ↓ AVR (superior and inferior branch) for post- vs. pretest and compared to CC at post-test
Saccadic eye movements			
Ayala et al. (2021) ⁹²	(1) Non-randomized trial with pretest/post-test comparisons (2) n.a. (3) Healthy younger adults (students) ■ $n = 16$ (8 females/8 males) ■ 22.9 ± 1.9 years (3.1) Recreationally active based on GLTEQ (63 ± 16 points) (3.2) n.r./n.r./n.r.	(1) Vigorous intensity (80% of predicted HR _{max}) and very light intensity in the warm-up and cool-down (50% of predicted HR _{max}) (2) 20 min (+ 2.5 min warm-up and cool down, respectively)	(1) Pro- and antisaccade task (2) ↓ Pro- and antisaccade RT from pretest to post-test
Dirk et al. (2020) ¹²²	(1) Non-randomized trial with within-subject crossover design and pretest/post-test comparisons (2) LUT vs. FOL phase of the menstrual cycle (3) Healthy younger women (students) ■ $n = 15$ (15 females) ■ 20.2 ± 0.7 years	(1) Moderate intensity (80% of estimated LT) * (2) 20 min (+ 4 min of warm-up and cool-down, respectively)	(1) Pro- and antisaccade task (2) ■ ↓ RT in antisaccade (but not prosaccade) RTs in LUT and FOL menstrual cycle phases from pretest to post-test

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Table 1 (Continued)

Study	Study design and sample characteristics	Characteristics of the physical interventions	Cognitive testing and main findings
Fujiwara et al. (2009) ¹⁰⁹	(3.1) 41.7 ± 3.8 kg/min (recreationally active) (3.2) n.r./58.0 ± 7.5 kg/n.r. (1) Cross-sectional study (2) Influence of expertise level (i.e., elite basketball players vs. skilled basketball players vs. non-athlete control) (3) Healthy younger adults (students) ■ $n = 27$ basketballs players (9 females/18 males; 13 elite and 14 skilled group); $n = 13$ non-athletes (5 females/8 males) ■ 20.3 ± 1.5 years (3.1) n.r. (3.2) n.r.	(1) n.a. (2) n.a.	(1) Pro- and antisaccade task (2) ■ ↓ Directional errors in antisaccade condition in ELI vs. SKI and CG ■ ↑ Positive and moderately high correlation in SKI and moderate correlation in CG between SL in prosaccade antisaccade condition
Heath et al. (2018) ¹²³	(1) RCT with within-subject cross-over design and pretest/post-test comparisons (2) Comparison of different exercise intensities (moderate vs. heavy vs. very heavy) (3) Healthy younger adults (university students) ■ $n = 12$ (5 females/7 males) ■ 22.7 ± 2.5 years (3.1) 45.0 ± 9.0 mL/kg/min (3.2) n.r./72.0 ± 13.0 kg/n.r.	(1) Moderate (80% of estimated LT), heavy (at 15% of the difference between the estimated LT and VO_{2peak}), very heavy (at 50% of the difference between their LT and VO_{2peak}), and light intensity in the warm-up (20 W) * (2) 10 min exercise (+ 3-min warm-up)	(1) Pro- and antisaccade task (2) ■ ↓ Antisaccade (but not prosaccade) SRTs from pretest to post-test ■ (–) No correlation between CRF level and the antisaccade RT difference scores (pre-minus post-test)
Heath et al. (2017) ¹¹⁸	(1) RCT between-subject design with pretest/post-test comparisons (2) Active CG (i.e., multi-modality (M2) and mind-motor intervention (M4)) (3) Older adults with self-reported cognitive complaints (community-dwelling) ■ $n = 63$ (47 females/16 males) ■ 67.0 ± 1.5 years (3.1) M2: 28.5 ± 7.6 mL/kg/min; M4: 28.0 ± 3.8 mL/kg/min (3.2) n.a./n.a./M2: 27.5 ± 4.7 kg/m²; M4: 28.0 ± 3.8 kg/m²	(1) Aerobic exercise at moderate-to-vigorous intensity (e.g., 65%–85% of predicted HR_{max}) (2) 60 min (including warm-up and cool-down of 5 min, respectively)	(1) Pro- and antisaccade task (2) ■ ↓ Antisaccade (but not prosaccade) RTs from pretest to post-test
Heath et al. (2020) ¹²⁴	(1) Non-randomized trial with pretest/post-test comparisons (2) Passive control (Experiment 2) (4) Healthy younger adults (students) ■ Experiment 1: $n = 18$ (10 females/8 males) ■ Experiment 2: $n = 36$ (20 females/16 males) ■ Experiment 1: EX 21.5 ± 2.2 years ■ Experiment 2: CG 22.6 ± 3.1 years (3.1) Recreationally active based on GLTEQ (59.0 ± 18.0 points) (3.2) n.r./n.r./n.r.	(1) Moderate intensity (80% of predicted HR_{max}) and very light intensity in the warm-up and cool-down (50% of predicted HR_{max}) (2) 20 min (+ 2.5-min warm-up and cool-down)	(1) Stimulus-driven and minimally delayed prosaccades ordered in an AABB task-switching paradigm (2) ■ ↓ RT switch-costs from pretest to post-test (i.e., in Experiment 1)
Heath et al. (2016) ¹¹⁹	(1) Non-randomized trial with between-subject design and pretest/post-test comparisons (2) HC (3) Older adults with/without objective cognitive impairments (community-dwelling) ■ OCI: $n = 12$ (8 females/4 males) ■ HC: $n = 11$ (9 females/2 males) ■ OCI: 72.3 ± 6.2 years ■ HC: 69.1 ± 5.6 years (3.1) OCI: 26.1 ± 6.1 mL/kg/min; HC: 29.6 ± 5.4 mL/kg/min (3.2) n.a./n.a./OCI: 29.3 ± 4.3 kg/m²; HC: 28.3 ± 3.2 kg/m²	(1) Light-to-moderate intensity (65%–85% of predicted HR_{max}) (2) 30 min (+ 5-min warm-up and cool-down, respectively)	(1) Pro- and antisaccade task (2) ■ ↓ antisaccade (but not prosaccade) RTs in OCI from pretest to post-test
Kokubu et al. (2006) ¹¹⁶	(1) Cross-sectional study (2) Comparison of athletes with different sports backgrounds (volleyball players vs. nonathletes) (3) Healthy younger adults (students)	(1) n.a. (2) n.a.	(1) Single saccade task, single key-press task, dual-task (i.e., both saccadic task and key-press task) (2) ■ ↓ Key-press RT in volleyball players

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Table 1 (Continued)

Study	Study design and sample characteristics	Characteristics of the physical interventions	Cognitive testing and main findings
Kunita et al. (2022) ¹¹⁴	■ Volleyball players: $n = 10$ (10 males) ■ Non-athletes: $n = 10$ (10 males), ■ Volleyball players: 20.1 ± 0.9 years ■ Non-athletes: 22.3 ± 1.3 years (3.1) Volleyball players: training 3 h per day/6 days per week; 6.6 ± 2.5 years of volleyball experience (3.2) Volleyball players 174.4 ± 4.8 cm; non-athletes: 169.9 ± 5.5 cm. Volleyball players: 65.9 ± 4.7 kg; non-athletes: 59.3 ± 2.9 kg (1) Cross-sectional study (2) Comparison of athletes with different sports backgrounds (table tennis vs. basketball vs. CG) (3) Healthy younger adults (students) ■ $n = 45$ (request) ■ Table tennis: $n = 15$ (n.r.) ■ Basketball: $n = 15$ (n.r.) ■ Control: $n = 15$ (n.r.) ■ Table tennis: $21.1 \pm$ n.r. years ■ Basketball: $20.8 \pm$ n.r. years ■ Table tennis: $20.4 \pm$ n.r. years (3.1) n.r. (3.2) n.r.	(1) n.a. (2) n.a.	- vs. nonathletes in the dual-task condition ■ (–) No statistically significant differences between groups concerning saccadic measures (1) Prosaccade task (2) ■ ↓ RT in the basketball and table tennis group vs. control group
Petrella et al. (2019) ¹²⁵	(1) RCT within-subject crossover design and pretest/post-test comparisons (2) Influence of different exercise intensities (i.e., moderate vs. heavy vs. very heavy) (3) Healthy older adults (community-dwelling) ■ $n = 17$ (9 females/12 males) ■ 73.0 ± 6.0 years (3.1) 31.0 ± 5.0 mL/kg/min (3.2) 169.0 ± 7.0 cm/71.0 ± 11.0 kg/25.0 ± 3.0 kg/m²	(1) Moderate (80% of estimated LT), heavy (at 15% of the difference between the estimated LT and VO_{2peak}), very heavy (at 50% of the difference between their LT and VO_{2peak}), and cool-down at standardized speed (1.2 mph at 0% grade) * (2) 10 min (+ 2-min warm-up and cool-down)	(1) Pro- and antisaccade task (2) ■ ↓ Antisaccade (but not prosaccade) RTs from pretest to post-test ■ (–) No correlation between exercise-induced changes in executive functions and CRF
Samani et al. (2018) ¹²⁶	(1) Non-randomized trial with within-subject crossover design and pretest/post-test comparisons (2) n.a. (3) Healthy young adults (students) ■ $n = 14$ (5 females/9 males) ■ 22.4 ± 2.0 years (3.1) Recreationally active based on GLETQ (68.0 ± 38.0 points) (3.2) n.r./n.r./n.r.	(1) Moderate-to-vigorous intensity (i.e., 60%–85% of predicted HR_{max}) and very light intensity warm-up (<50% of predicted HR_{max}) (2) 10 min (+ 2.5-min warm-up and 2.5-min cool-down period)	(1) Pro- and antisaccade task (2) ■ ↓ Antisaccade (but not prosaccade) RT and CV from pretest to post-test
Shaw et al. (2022) ¹³⁷	(1) Non-randomized trial with between-subject design and pretest/post-test comparisons (2) Passive CG (3) Healthy younger adults ■ EG: $n = 30$ (30 males) ■ CG: $n = 31$ (31 males) ■ 23.11 ± 3.02 years (3.1) n.r. (3.2) n.r.	(1) GXT (i.e., initially walked at 2.0 km/h and 1% grade for 2 min, increased to 5.5 km/h, with 0.2 km/h increments every 15 s, the grade was kept constant until 16 km/h was reached, at which point grade increments increased by 0.5% every 30 s) (2) Until meeting HR_{max}	(1) Prosaccade task ■ ↑ Number of processed items in EG and CG (post- vs. pretest)
Shellington et al. (2018) ¹²¹	- RCT with between-subject design and pretest/post-test comparisons (2) Passive CG (3) Middle-aged and older adults with type 2 diabetes and self-reported cognitive complaints ■ SSE: $n = 12$ (4 females/8 males) ■ CG: $n = 13$ (4 females/9 males) ■ SSE: 65.9 ± 5.2 years ■ CG: 71.2 ± 6.9 years (3.1) n.a.	(1) Low intensity* (2) 60 min (including 5–10-min warm-up + 5–10-min cool-down)	- Pro- and antisaccade task, Montreal Cognitive Assessment, Clock Drawing test, and Cambridge Brain Sciences cognitive test battery (2) ■ (–) No statistically significant changes in pre- to post-test of pro- and antisaccade performance metrics

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Table 1 (Continued)

Study	Study design and sample characteristics	Characteristics of the physical interventions	Cognitive testing and main findings
Shirzad et al. (2012) ¹²⁷	(3.2) SSE 170.0 ± 10.0 cm; CG 170.0 ± 10.0 cm; SSE: 94.5 ± 19.6 kg; CG: 88.4 ± 11.4 kg; SSE: 33.3 ± 4.8 kg/m ² ; CG: 31.9 ± 4.6 kg/m ² (1) RCT with within-subject design and pretest/post-test comparisons (2) Passive exercise CC (i.e., mechanically driven cycle ergometer) and passive CC (i.e., seated rest) (3) Healthy younger adults (students) ■ $n = 28$ (11 females/17 males) ■ 22.3 ± 2.0 years (3.1) Recreationally active based on GLETQ (62.0 ± 26.0 points) (3.2) n.r./n.r./n.r.	(1) Light intensity (37 W) * (2) 20 min (+ 2 min warm-up and cool-down, respectively)	(1) Pro- and antisaccade task (2) ■ ↓ antisaccade (but not prosaccade) RT from pretest to post-test ■ ↓ Negative and low correlation between steady-state BVs and post-exercise antisaccade RTs
Shukla et al. (2020) ¹²⁸	(1) Non-randomized trial with pretest/post-test comparisons (2) Passive CG (i.e., seated rest - Experiment 2) (3) Healthy younger adults (students) ■ $n = 35$ (19 females/16 males) ■ Experiment 1: EX: $n = 20$ (11 females/9 males) ■ Experiment 2: CG: $n = 15$ (8 females/7 males) ■ Experiment 1: EX: 21.3 ± 18.0 years ■ Experiment 2: CG: 20.3 ± 2.3 years (3.1) Recreationally active based on GLETQ (EX: 65.0 ± 17.0 points; CG: 59.0 ± 18.0 points) (3.2) n.r./n.r./n.r.	(1) Moderate intensity (80% of predicted HR _{max}) and very light intensity (<50% of predicted HR _{max}) (2) 20 min (+ 2.5 min warm-up and cool-down, respectively)	(1) Pro- and antisaccades ordered in an AABB task-switching paradigm (2) ■ ↓ RT switch-costs from pretest to post-test (i.e., in Experiment 1)
Shukla et al. (2022) ¹²⁹	(1) Non-randomized trial with pretest/post-test comparisons (2) Passive CG (i.e., seated rest - Experiment 2) (3) Healthy younger adults (university students) ■ Experiment 1: $n = 20$ (11 females/9 males) ■ Experiment 2: $n = 19$ (10 females/9 males) ■ Experiment 1: EX: 22.5 ± 2.5 years ■ Experiment 2: CG: 22.2 ± 1.9 years (3.1) Recreationally active based on GLETQ (EX: 60.0 ± 19.0 points; CG: 68.0 ± 24.0 points) (3.2) n.r./n.r./n.r.	(1) Vigorous intensity (80% of predicted HR _{max}) and very light intensity warm-up and cool-down (<50% of predicted HR _{max}) (2) 20 min (+ 2.5 min warm-up and cool-down)	(1) Stimulus-driven and minimally delayed saccade task arranged in an AABB task-switching paradigm (2) ■ ↓ RT switch-costs from pretest to post-test (i.e., immediately and 30 min after exercise cessation)
Tari et al. (2021) ¹³⁰	(1) Non-randomized trial with within-subject design and pretest/post-test comparisons (2) Comparison of different exercise intensities (i.e., light vs. moderate vs. heavy) (3) Healthy younger adults (students) ■ $n = 16$ (5 females/11 males) ■ 22.8 ± 1.6 years (3.1) Cardiorespiratory fitness: 2.66 ± 0.75 L/min/ recreationally active based on GLETQ (51.0 ± 21.0 points) (3.2) 171.9 ± 10.4 cm/ 72.0 ± 13.5 kg/n.r.	(1) Light intensity (25 W), moderate intensity (80% of estimated LT), and heavy intensity (15% of the difference between participant-specific estimated LT and VO _{2peak}) * (2) 10 min (+ 6-min warm-up)	(1) Pro- and antisaccade task (2) ■ ↓ Antisaccade (but not prosaccade) RT from pretest to post-test ■ (–) No statistically significant correlations between antisaccade RT difference scores and cortical hemodynamic measure
Tari et al. (2020) ¹³¹	(1) Non-randomized trial with within-subject design and pretest/post-test comparisons (2) Passive CC (e.g., hypercapnic environment) (3) Healthy younger adults (students) ■ $n = 16$ (7 females/9 males) ■ 22.8 ± 2.3 years (3.1) Recreationally active based on GLETQ (65.0 ± 25.0 points) (3.2) n.r./n.r./n.r.	(1) Moderate-to-vigorous intensity (intensity corresponding to participants' elevated steady-state PETCO ₂ during the hypercapnic condition) and standardized warm-up (25 W) * (2) 10 min (+ 6-min warm-up)	(1) Pro- and antisaccade task (2) ■ ↓ Antisaccade (but not prosaccade) RT in EX and hypercapnic condition from pretest to post-test ■ ↑ Moderate and positive correlation between RT and blood velocity difference in EX
Tsai et al. (2021) ¹³³	(1) RCT with within-subject cross-over design and pretest/post-test comparisons	(1) Vigorous intensity in HIIE (70%–75% of HRR in working bout/	(1) Pro- and antisaccade task (2) ■ ↓ RT in antisaccade (but not

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Table 1 (Continued)

Study	Study design and sample characteristics	Characteristics of the physical interventions	Cognitive testing and main findings
	(2) Comparison of different exercise protocols (HIIE vs. MICE) and CG (i.e., seated rest) (3) Healthy older adults (community-dwelling) ■ $n = 20$ (10 females/10 males) ■ 61.2 ± 4.4 years (3.1) 35.6 ± 5.5 mL/kg/min (3.2) 162.9 ± 7.9 cm/ 64.3 ± 7.6 kg/ 24.2 ± 2.3 kg/m ²	RPE 9–11 in recovery bout) and moderate intensity in MICE (50%–55% of HRR), light intensity in the warm-up and cool down (RPE 9–11) (2) 30 min consisting of 24 min of the main exercise (e.g., HIIE 1 min working bout alternating with 2 min of active recovery) + 4 min warm-up and 2 min cool-down	prosaccade condition) condition in HIIE and MICE from pretest to post-test ■ ↓ Saccadic peak velocity in prosaccade condition and antisaccade condition in HIIE from pretest to post-test
Yilmaz et al. (2018) ¹¹⁰	(1) Cross-sectional study (2) Comparison of athletes with different sports backgrounds (tennis vs. volleyball vs. basketball vs. swimmers vs. CG) (4) Healthy younger adults ■ $n = 50$ (50 males) ■ Tennis: 21.9 ± 1.4 years ■ Volleyball: 21.6 ± 1.6 years ■ Basketball: 22.1 ± 1.5 years ■ Swimmers: 22.1 ± 1.5 years (3.1) n.r. (3.2) n.r.	(1) n.a. (2) n.a.	(1) Pro- and antisaccade task (2) ■ ↓ RT in antisaccade condition in tennis players vs. swimmers and non-athletes, volleyball players vs. swimmers and non-athletes, basketball players vs. non-athletes ■ ↑ Prosaccade velocity in tennis players vs. basketball players, swimmers, and non-athletes; and volleyball players vs. non-athletes
Zhou et al. (2022) ¹³⁴	(1) RCT with between-subject design and pretest/post-test comparisons (2) Passive CG (3) Younger adults (students) with mobile phone addiction ■ EX: $n = 15$ (12 females/3 males) ■ CON: $n = 15$ (11 females/4 males) ■ EX: 19.5 ± 0.72 years ■ CON: 18.9 ± 0.93 years (3.1) EX: 1298.8 ± 1633.0 MET per week; CG: 1060.5 ± 1636.4 MET per week (3.2) EX: 163.0 ± 7.7 cm; CG: 165.4 ± 8.2 cm/ 51.8 ± 6.5 kg; CG: 68.9 ± 24.9 kg/EX: 19.4 ± 1.4 kg/m ² ; CG: 24.9 ± 2.9 kg/m ²	(1) Light-to-moderate intensity (i.e., 60%–70% of predicted HR _{max}) (2) 15 min	(1) Antisaccade task (2) ■ ↓ Directional errors in EX and CON (post- vs. pretest) ■ ↓ RT in CON but not in EX (post- vs. pretest)
Zhou (2021) ¹¹⁵	(1) Cross-sectional study (2) Skilled vs. less-skilled soccer players (3) Healthy female adolescent soccer players ■ $n = 56$ (16.50 ± 0.71 years) ■ Skilled soccer players: $n = 24$ (24 females) ■ Less-skilled soccer players: $n = 32$ (32 females) ■ Skilled soccer players: 16.6 ± 0.7 years ■ Less-skilled soccer players: 16.4 ± 0.7 years (3.1) n.a. (3.2) n.a.	(1) n.a. (2) n.a.	(1) Prosaccade task (2) ■ ↓ RT and variability of RT (skilled vs. less-skilled soccer players) ■ ↑ Spatial accuracy (skilled vs. less-skilled soccer players)
Spontaneous eye blink rate			
Kuwamizu et al. (2021) ⁹⁵	(1) Cross-sectional study (2) Influence of CRF (3) Healthy younger adults ■ $n = 35$ (35 males) ■ 20.9 ± 1.8 years (3.1) 44.7 ± 7.9 mL/kg/min (3.2) 173.2 ± 4.5 cm/ 64.3 ± 8.2 kg/ 21.4 ± 2.6 kg/m ²	(1) n.a. (2) n.a.	(1) Modified Stroop task (2) ■ ↓ Negative low correlation between Stroop interference and CRF (adjusted for age and BMI) ■ ↓ Negative moderate correlation between Stroop interference and resting state spontaneous eye blink rate (adjusted for age and BMI) ■ ↑ Positive low correlation between spontaneous eye blink rate and CRF (adjusted for age and BMI) ■ ↑ Positive low correlation between resting-state spontaneous eye blink rate and neural efficiency score (adjusted for age and BMI)

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Table 1 (Continued)

Study	Study design and sample characteristics	Characteristics of the physical interventions	Cognitive testing and main findings
			■ ↑ correlation between CRF and Stroop interference performance is mediated by resting-state spontaneous eye blink rate (adjusted for age and BMI)

Notes: Data are shown as mean $\pm$ SD. ↑ indicates a statistically significant increase or positive correlation; ↓ indicates a statistically significant decrease or negative correlation; (–) indicates the absence of a statistically significant change or correlation. Please note that we rated exercise intensity based on the classification approach provided by Garber et al.¹⁸⁸ where possible (studies for which it was not possible to utilize this approach were marked with an *). We rated the magnitude of the correlation coefficients as follows: no correlation <0.19 , low correlation ≥ 0.19 to ≤ 0.39 , moderate correlation >0.39 to ≤ 0.59 , moderately high correlation >0.59 to ≤ 0.79 , and high correlation >0.79 .^{189,190}

In the study done by Roeh and colleagues,¹¹² ^a chronic effects are based on the cross-sectional data, whereas ^b acute effects are based on the measurements being conducted within 2 h after an individual's completion of the marathon.

Abbreviations: AVR = arteriolar-to-venular ratio; BMI = body mass index; CC = control condition; CG = control group; CRAE = central retinal arteriolar equivalent; CRF = cardiorespiratory fitness level; CRVE = central retinal venular equivalent; CV = coefficient of variation; ELI = elite basketball players; EX = exercise condition/exercise group; FOL = early-follicular; GLTEQ = Godin Leisure-Time Exercise Questionnaire; GXT = graded exercise test; HIIE = high-intensity interval exercise; HR_{max} = maximal heart rate; HRR = heart rate reserve; LT = lactate threshold; LUT = mid-luteal; MET = metabolic equivalent of task; MICE = moderate-intensity continuous exercise; mph = miles per hour; MVPA = moderate-to-vigorous physical activity; n.a. = not applicable; n.r. = not reported; OCI = objective cognitive impairment; PA = physically active; PETCO₂ = partial pressure of exhaled carbon dioxide; PIA = physically inactive; RPE = rating of perceived exertion; RT = reaction time (note that in some studies using saccade tasks *reaction time* is also referred to as *saccade latency*); SKI = skilled basketball players; SSE = square-stepping exercise; TMT = Trail Making Test; TW-YMCA = total work Young Men's Christian Association; VO_{2peak} = peak oxygen uptake during a graded exercise test.

with regular physical activity level.¹¹¹ However, Chandler and colleagues⁹⁴ observed that a higher level of cardiorespiratory fitness was associated with shorter reaction time (i.e., assessed during a modified Flanker task probing executive functioning) in the 126 healthy college students they recruited. However, they did not observe a correlation between cardiorespiratory fitness level and phasic pupil size, nor did they find evidence for a mediating effect of phasic pupil size between cardiorespiratory fitness level and reaction time. An additional cross-sectional study noted that a decrease in phasic pupil size was more pronounced with higher levels of physical activity when viewing a physical activity stimulus compared to a physical inactivity stimulus.¹¹⁷

Two studies investigated the effect of acute endurance exercise.^{93,132} One observed no change in tonic pupil size (i.e., assessed at rest) or phasic pupil size (i.e., assessed during a cognitive task) after moderate-intensity exercise,¹³² and the other observed increased tonic pupil size after light-to-moderate intensity exercise compared to a control condition.⁹³ Concerning the comparison of the pretest to the post-test, 1 study reported a decrease in tonic pupil size and an increase of phasic pupil size after a bout of vigorous-intensity endurance exercise,⁹² whereas another did not observe a significant change in tonic pupil size or increase in phasic pupil size after a bout of moderate-intensity endurance exercise.¹³² A more detailed overview of the main findings is provided in Table 1.

3.4.3. Retinal vessel analysis

Two of the reviewed studies used retinal vessel analysis.^{96,112} In 1 study,⁹⁶ 35 adolescents were randomly allocated to either a 12-week exercise or active control intervention (i.e., social interaction). After the 12-week intervention period, the exercise group had (a) a significantly shorter reaction time during the incongruent condition of the Stroop task, and (b) a greater central retinal arteriolar equivalent when compared to the active control

group.⁹⁶ Moreover, a negative and moderate correlation between the reaction time change score and central retinal arteriolar equivalent was observed.⁹⁶ This finding suggests that improvements in inhibitory control are associated with the widening of arterioles, and although such a correlation does not necessarily imply causation, it does support the idea that physical-exercise-induced cognitive improvements may be due, in part, to changes in cerebrovascular structure/function, as is hypothesized in the literature.^{13,34,36,75}

In the other study, researchers investigated the chronic effects of marathon running on cognitive measures and retinal vascularization among middle-aged adults.¹¹² The following chronic effects were observed: (a) a positive correlation between the discriminability index (i.e., a measure to discriminate between targets and irrelevant stimuli) in a 3-Back task and the arteriolar-to-venular ratio and a negative correlation between the discriminability index in a 3-Back task and the central retinal venular equivalent, and (b) a negative correlation between time to complete the Trail Making Test B and central retinal arteriolar equivalent. Concerning the acute effects of exercise, for which measurements were conducted within 2 h of the completion of the marathon, a positive correlation between the d2 concentration performance (i.e., the difference between correct and incorrect marked letters) and central retinal arteriolar equivalent and a negative correlation between the discriminability index in a 1-Back task and time to complete Trail Making Test A with central retinal venular equivalent were observed. Another study observed a higher diameter of the superior and inferior branches of the temporal retinal arterial venules and a lower arteriolar-to-venular diameter ratio after an acute bout of high-intensity interval boxing exercise; the latter was also significantly lower compared to post-test values of the passive control group.¹³⁶ Those changes were accompanied by an improvement in reaction time on the procedural reaction time test and go/no-go test in the exercise condition but not in the control condition (i.e., seated rest).¹³⁶

Two additional studies used optical coherence tomography to study the association between measures of retinal vessels, cognition, and the influence of physical fitness¹¹³ or physical exercise.¹²⁰ In a cross-sectional study, a moderately high and positive correlation between the Montreal Cognitive Assessment score and vessel density of the retinal vascular network and superficial vascular plexus (adjusted for age, sex, education, and body mass index) was observed, but no association to physical fitness was noticed.¹¹³ In another study, it was observed that changes in the retinal vessel density of the superficial vascular plexus are moderately and negatively correlated with changes in the Fluid Cognition Composite Score and List Sorting Working Memory Test after an 8-week-long high-speed circuit resistance training intervention in healthy older adults.¹²⁰

Taken together, the majority of the reviewed studies observed that an exercise-induced change of the retinal vascular status (e.g., higher arteriolar-to-venular ratio, wider central retinal arteriolar equivalent, and narrower central retinal venular equivalent) is correlated with better cognitive performance. Thus, these results at least partly support the idea that physical exercise-induced improvements in cognitive performance might be related to positive changes in the status of the cerebrovascular system (i.e., operationalized by measures of the retinal vessels).^{13,34,36,75}

3.4.4. Saccadic eye movements

Four cross-sectional studies focused on saccadic eye movements, with researchers either examining whether saccadic eye movements varied as a function of the level of regular physical activity¹¹¹ or the expertise/skill level in specific sports disciplines (e.g., amateur athletes vs. elite athletes).^{109,110,115} In particular, Zhou and colleagues¹¹¹ reported that younger adults with a higher level of regular physical activity exhibited shorter saccade reaction times (also referred to as saccade latency) and lower error rates in the antisaccade task compared to physically inactive adults. Furthermore, in the studies conducted by Fujiwara et al.¹⁰⁹ and Yilmaz et al.¹¹⁰ utilizing prosaccade and antisaccade tasks, antisaccade directional errors and prosaccade velocities varied as a function of skill level and sport discipline. In particular, elite athletes made fewer antisaccade directional errors compared to amateur athletes and controls¹⁰⁹ or had a shorter prosaccade reaction time¹¹⁴ (see Table 1 for more details). In turn, Kokubu and colleagues¹¹⁶ observed that volleyball players exhibited shorter dual-task prosaccade reaction times as compared to nonathletes.¹¹⁶ In addition, Zhou¹¹⁵ reported that skilled soccer players had shorter and less variable prosaccade reaction times and more accurate endpoints relative to less-skilled soccer players.

In acute physical exercise studies using a between- or within-participant design, the following outcome parameters were observed from pre- to post-test: (a) reaction times showed a selective postexercise decrease for antisaccades but not prosaccades^{122,123,125,126,130,131,133} or showed decreased reaction times for antisaccades and prosaccades,⁹² (b) decreased coefficient of variation of saccade reaction times,^{126,127} (c) lower number of directional errors in antisaccade condition,¹³⁴ (d) decreased prosaccade (but not antisaccade) difference score,¹²⁸ (e) decreased switch cost operationalized by difference scores of saccade reaction times (i.e., task-switch minus task-repeat),¹²⁹

and (f) shorter saccadic peak velocities.¹³³ One study found a significant increase in the stimulus-driven saccade difference scores from the pretest to the post-test after an acute bout of moderate-intensity endurance exercise.¹²⁴ Another study using a saccadic eye movement chart reported improvements in the visual performance in both the group that performed a graded exercise test and the passive control group.¹³⁷

With respect to 24-week-long physical interventions, anti-saccade (but not pro-saccade) reaction time decreased from pretest to post-test,^{118,119} although there was 1 study that did not observe these changes.¹²¹ In general, the above-presented findings suggest that acute bouts of physical exercise, as well as long-term physical training, can positively influence executive functioning as measured by the antisaccade task.

Concerning associations of saccadic eye measures with other parameters, Tari et al.¹³¹ reported a moderate, positive correlation between post-exercise antisaccade reaction time and cerebral blood velocity (as monitored via fNIRS and transcranial Doppler ultrasound of the middle cerebral artery) in the exercise group, whereas Shirzad et al.¹²⁷ reported a negative correlation between the aforementioned variables.¹²⁷ Although both findings suggest that increases in cerebral blood flow, among other factors, might be a potential mechanism driving post-exercise benefits in executive function (operationalized by an antisaccade task), more research is necessary to provide empirical support for the assumption and to elucidate the relationships between cerebral blood flow changes and other neurobiological mechanisms relevant for cognition (e.g., neurovascular coupling and neural activity).^{5,140} A more detailed overview of the main findings of the reviewed studies with respect to saccadic eye movements is provided in Table 1.

3.4.5. Spontaneous eye blink rate

Based on the hypothesis that the brain's dopaminergic system might act as a mediator of physical activity- and physical fitness-induced changes in cognitive performance, 1 cross-sectional study examined whether resting-state spontaneous eye blink rate (as an eye-based marker thought to reflect the activity of the dopaminergic system) mediated the relationship between the cardiorespiratory fitness level and executive function.⁹⁵ This study observed (a) a small, negative correlation between Stroop interference (operationalized by inverse efficiency score) and cardiorespiratory fitness level, (b) a moderate, negative correlation between Stroop interference and the resting-state spontaneous eye blink rate, and (c) a small, positive correlation between the resting-state spontaneous eye blink rate and cardiorespiratory fitness level.⁹⁵ Furthermore, the study examined the physiological implication of spontaneous eye blink rate in terms of the neural efficiency score of the left dorsolateral prefrontal cortex using fNIRS (calculated as described in Refs. 141 and 142) and observed that higher resting-state spontaneous eye blink rate was correlated with a higher neural efficiency score of the left dorsolateral prefrontal cortex.⁹⁵ Taken together, these findings suggest that a higher level of cardiorespiratory fitness may be linked to better executive function with neural efficiency of the left dorsolateral prefrontal cortex (as measured by fNIRS during a Stroop task) and that the link is partly mediated by brain dopaminergic regulation (operationalized via resting-state spontaneous eye blink rate).

3.5. Assessment of methodological quality

The methodological quality of the cross-sectional studies was assessed using the Joanna Briggs Institute tool.¹⁰⁶ Most of these studies have a relatively low risk for bias concerning the majority of the items (see the [Supplementary materials](#) for a detailed overview). In 5 studies, potential confounders were not appropriately identified and dealt with (Items 5 and 6), so some risk of bias is present.^{109,110,114–116}

Regarding interventional studies (i.e., acute and chronic physical exercise studies), a modified version of the TESTEX scale was used to assess the risk of bias.¹⁰⁵ Please note that due to the inclusion of acute physical exercise studies with pretest/post-test comparisons utilizing a single group design (Item 2 = randomization, Item 4 = similar baseline, and Item 10 = between-group/condition analysis) and randomized cross-over controlled within-subject design (Item 12 = monitoring physical activity level and Item 13 = relative/constant exercise intensity), some items are rated as “not applicable”. Furthermore, attendance adherence and adverse events are not typically relevant during acute physical exercise studies and, thus, these 2 items are also considered “not applicable”. In general, most of the interventional studies were rated as having a low risk of bias in the majority of categories (for a detailed overview see the [Supplementary materials](#)). Concerning the blinding (Item 5), the majority of the reviewed acute physical exercise studies were rated as having an unclear risk of bias.^{92,122–133,135} This is most likely explained by the fact that assessments are computerized, which means there is little to no opportunity for the assessor to influence the outcome even though the person who initialized the cognitive tests on the computer was not blinded.

4. Discussion

This systematic review aimed to comprehensively evaluate the current state of the literature examining the associations between physical activity, fitness, cognitive performance, and eye-based measures. The main findings of this systematic review are as follows: (a) there is insufficient evidence available to draw solid conclusions concerning gaze-fixation-based measures; (b) the evidence that pupillometric measures, as a proxy of the noradrenergic system, can explain the positive effect of acute physical exercises and cardiorespiratory fitness on cognitive performance is mixed; (c) physical training- or fitness-related changes of the cerebrovascular system (operationalized via changes in retinal vasculature) are, in general, positively associated with cognitive performance improvements; (d) acute and chronic physical exercises have a positive effect on oculomotor measures of executive functions (operationalized via the antisaccade tasks); and (e) the positive association between cardiorespiratory fitness and cognitive performance is partly mediated by the dopaminergic system (operationalized via spontaneous eye-blink rate). We discuss these findings in more detail below.

4.1. Fixation

The findings from the cross-sectional study provide some evidence that the attentional bias toward physical activity stimuli

is more pronounced in individuals with higher levels of physical activity.¹¹⁷ In addition, acute exercise does not appear to improve attentional processes with regard to facial expression tasks,¹³⁵ which is in contrast to available evidence showing that physical exercise can improve certain aspects of social cognition (e.g., facial emotion labeling and matching performance).¹⁴³ However, given that there is a limited number of studies ($n = 2$) using gaze-fixation measures in the field of exercise cognition, these findings should be treated as preliminary. Further research is necessary to draw more definite conclusions.

4.2. Pupillometry

The reviewed studies investigated the effects of (a) physical activity level,¹¹¹ (b) cardiorespiratory fitness level,^{94,108} and (c) acute bouts of physical exercise^{92,93,132} on pupillometric indices and cognitive performance. In general, the cross-sectional studies reported a positive association between phasic pupil size and cardiorespiratory fitness level,^{93,108} whereas tonic pupil size was positively associated with the level of regular physical activity.¹¹¹ Currently, however, there is no convincing evidence available that pupillometric indices (i.e., pupil size) as a proxy of arousal-induced changes in specific neurobiological systems (e.g., noradrenergic system) mediate the positive relationship between physical fitness and cognitive performance.⁹⁴ This finding may be related to the fact that (tonic) pupillometric indices are indirect markers of changes in specific neurobiological systems (e.g., noradrenergic system) and, thus, are only weakly correlated with measures of cognitive performance.^{144–147}

With respect to the effects of an acute bout of physical exercise on pupillometric indices, the current evidence is mixed. Some studies observed no change in tonic or phasic pupil size after moderate-intensity exercise,¹³² others found an increase in tonic pupil size after light-to-moderate intensity exercise⁹³ or a decrease in tonic pupil size and an increase in phasic pupil size after vigorous-intensity exercise.⁹² Such inconsistent findings suggest that exercise intensity differentially influences pupil size, which is a proxy of physiological and psychological arousal. Exercise-intensity dependent effects on pupillometric indices have only started to be explored^{148,149} but, in general, available studies suggest that pupil dilatation increases with higher exercise intensities^{148,149} and decreases relatively gradually following exercise cessation (depending on environmental illumination).¹⁴⁹

In summary, while the evidence suggests that tonic and phasic pupillometric indices can be modulated by (a) regular physical activity, (b) cardiorespiratory fitness, and (c) an acute bout of physical exercise, we did not find compelling evidence that pupillometric measures are associated with cognitive performance. Since current evidence on the relationships between pupillometric indices, physical activity and/or physical fitness, and cognitive performance is limited ($n = 6$), further research is necessary to broaden our knowledge base.

4.3. Retinal vessel analysis

In the reviewed studies, static retinal vessel analysis and optical coherence tomography angiography were used to assess the relationship between eye-based measures, cognitive

performance, and (a) cardiorespiratory fitness,¹¹³ (b) acute physical exercise,¹³⁶ and (c) chronic physical exercise.^{96,120} The findings of the studies suggest that a positive modification of the retinal vascular status (e.g., higher arteriolar-to-venular ratio, wider central retinal arteriolar equivalent, and narrower central retinal venular equivalent) in response to acute¹³⁶ and chronic^{96,120} physical exercise is linked to better cognitive performance. However, in a cross-sectional study in older adults, no relationship between cardiorespiratory fitness, measures of global cognitive performance, and measures of the retinal vessels was observed.¹¹³ The absence of a positive relationship between cardiorespiratory fitness and global cognitive performance might be related to the small sample size of the study ($n = 20$) or to the possibility that some vascular disease associated with aging makes it difficult to detect a relationship of a smaller magnitude.¹¹³ On the other hand, observations from the interventional studies demonstrated a positive relationship between exercise-induced changes in the retinal vasculature and cognitive performance, which is in line with existing findings that indicate regular physical activity (e.g., in form of physical exercise) and physical fitness can positively influence vascular retinal parameters¹⁵⁰ and that a relationship between vascular retinal parameters and cognitive performance exists in (a) children,^{97,151–153} (b) patients with psychiatric diseases,¹⁵⁴ (c) older adults (i.e., measures of cognitive performance¹⁵⁵ and cognitive decline^{156–159}), and (d) older adults who are at a higher risk for developing neurological diseases (e.g., vascular dementia,¹⁶⁰ Alzheimer's disease^{161–163}). However, other observational studies did not observe statistically significant correlations between vascular retinal parameters and cognitive performance in older adults,^{164–166} suggesting that some other factors might moderate their relationship (e.g., age or assessed cognitive domain).

In summary, the findings of the reviewed studies support established hypotheses (e.g., cardiovascular fitness hypothesis,^{13,33–35} cerebrovascular reserve hypothesis³⁶) attempting to explain how physical activity- or physical fitness-related changes in the cerebrovascular system play a role in the improvement of cognitive performance.

4.4. Saccadic eye movements

The cross-sectional studies provided evidence to suggest that in younger adults (a) higher levels of regular physical activity¹¹¹ and (b) higher sport-specific skill levels (i.e., elite athlete vs. amateur athlete or non-athlete)^{109,110,114–116} are linked to superior pro- and antisaccade tasks (e.g., shorter reaction time and fewer directional errors). In general, these findings are in agreement with the current literature, which demonstrates that higher levels of regular physical activity¹⁶⁷ and sport-specific skills¹⁶⁸ are associated with superior cognitive performance.

In addition, the majority of studies investigating the influence of an acute bout of physical exercise in healthy younger and older adults observed a selective reduction in antisaccade-but not prosaccade-reaction times^{122,123,125,126,130,131,133} and an improvement in other performance metrics (e.g., a decrease of coefficient of variation of saccadic latencies,^{126,127} antisaccade directional errors,¹³⁴ and task-switch costs^{128,129}) at the post-test, suggesting

that acute bouts of physical exercise can improve cognitive performance (operationalized via eye-based measures). Again, this finding agrees with the available literature on the topic.^{4,5,169} It is worth noting that 2 studies reported a correlation between exercise-induced cerebral blood flow changes and antisaccade reaction time,^{127,131} which supports the idea that exercise-induced changes in cerebral blood flow may contribute, among other factors, to improved cognitive performance following an acute bout of physical exercise.⁵ However, given that neither the relationship between acute exercise-induced changes in cerebral blood flow and post-exercise cognitive performance improvements nor the relationship between acute physical exercise-induced changes in cerebral blood flow and other neurobiological mechanisms relevant for cognition (e.g., neurovascular coupling and neural activity) are fully understood,^{5,140} further research is necessary.

With respect to physical training interventions, it was found that antisaccade-but not prosaccade-reaction times decreased from pretest to post-test during a 24-week long intervention period in older adults with and without cognitive impairments;^{118,119} however, this finding was not universal.¹²¹ In general, these results reinforce those of previous reviews in the field,^{2,99,170} which have suggested that physical training can positively influence executive functions (operationalized via eye-based saccadic measures) in older adults.

Taken together, the findings show that higher levels of regular physical activity and sport-specific skills, as well as acute bouts of physical exercise and physical training, are linked to better saccadic performance. Our results complement the existing literature by documenting that language-free measures of cognitive performance (e.g., saccadic measures) can be positively modulated by regular physical activity and physical fitness.

4.5. Spontaneous eye blink rate

One cross-sectional study noted that in younger adults a higher level of cardiorespiratory fitness is linked to better executive function with neural efficiency of the left dorsolateral prefrontal cortex (as measured by fNIRS during a Stroop task) and that this link is partly mediated by the brain dopaminergic regulation (operationalized via phasic spontaneous eye blink rate).⁹⁵ This finding complements the current literature on the modulating role of physical activity, the dopaminergic system, and cognitive performance. In particular, recent investigations using positron emission tomography suggest that, especially in older adults, higher levels (operationalized via steps per day)^{171,172} and a higher intensity of physical activity,¹⁷³ as well as a higher level of cardiorespiratory fitness,¹⁷⁴ can positively influence the dopaminergic system. However, only 2 of the aforementioned studies observed a positive association between the dopaminergic system and cognitive performance (i.e., episodic and working memory, global cognition),^{172,173} while 1 study assessing working memory performance did not observe such a relationship.¹⁷⁴

In summary, the research investigating whether modulations of the dopaminergic system mediate the positive relationship of physical activity and physical fitness to cognitive performance is relatively heterogeneous. The assessment of tonic and phasic spontaneous eye blink rate, on its own or in combination with

neuroimaging modalities, is a promising utility for broadening our knowledge of the neurobiological mechanisms of the exercise-cognition interaction in general and of the role of the dopaminergic system in particular. Still, further research is needed (e.g., on the psychometric properties of tonic and phasic spontaneous eye blink rate) before more solid conclusions can be drawn.

4.6. Risk of bias

In general, the risk of bias in the reviewed studies is low in most categories. Our risk of bias assessment indicates that some of the cross-sectional studies did not sufficiently control for potential confounders. Thus, further studies should aim for more rigorous control of potential confounders to strengthen the analysis and, in turn, the robustness of the findings. Most of the acute physical exercise studies were rated as having an unclear risk of bias with respect to Item 5: blinding. This is related to the fact that the assessor was not blinded but the cognitive testing was computerized, which allowed—at least in theory—for little to no manipulation of the cognitive assessments. To optimize the risk of bias assessment in acute physical exercise studies, it may be beneficial, in our opinion, to develop a more specific risk of bias assessment instrument for this application, as such an instrument is currently not available to the best of our knowledge.

5. Limitations

5.1. Limitations of eye-based measures

Since eye-based measures are indirect markers for changes in the brain that can be influenced by other confounders and/or complex neurobiological processes, it should be acknowledged that their validity for reflecting certain outcomes of interest could be somewhat limited. For instance, recent findings imply that changes in pupil dilation (assessed via pupillometry) not only reflect arousal-related brain changes in the noradrenergic system (i.e., locus-coeruleus via norepinephrine release),^{5,27} but that they might be the result of a rather complex interplay of different neural systems^{25,45,46}—including, for example, the cholinergic system in the basal forebrain.⁴⁷ Thus, future research (e.g., basic research in animals) should aim to disentangle the complex neurobiological mechanisms contributing to changes in eye-based measures to allow for a more robust and nuanced interpretation of these measures in general and in the field of exercise-cognition in particular. Furthermore, eye-based measures can be influenced by environmental conditions (e.g., environmental luminance); thus, a relatively high standardization of the experimental procedures is required.^{175–177}

5.2. Limitations of this systematic review

This systematic review has several limitations, which should be considered. First, the bias of some reviewed studies was rated as unclear because the authors did not respond to repeated requests. This could somewhat bias our methodological quality assessment and, in turn, interpretation of the findings of the reviewed studies. Second, given that the number of available studies is limited and that the reviewed studies are

somewhat heterogeneous with respect to study characteristics (e.g., exercise and training characteristics), it is difficult to draw robust and nuanced conclusions or to conduct a meta-analysis. Finally, we only included studies written in English, excluding potentially relevant studies published in other languages. Our results should be interpreted in light of these limitations.

6. Recommendations for future research

Our systematic review revealed that the majority of reviewed studies were conducted in healthy younger adults^{92–95,108–111,116,122–124,126–132,135,136} and older adults,^{113,120} whereas the number of studies investigating special cohorts, such as older adults with subjective¹¹⁸ and objective cognitive impairments,¹¹⁹ was considerably lower. Based on the aforementioned findings, further research in lesser-studied cohorts (e.g., children, middle-aged adults, and older adults with diseases) is needed to expand our knowledge of how eye-based measures may help us uncover the positive relationship between physical activity and physical fitness, on the one hand, and cognitive performance on the other.

Furthermore, our systematic review revealed that the majority of relevant cross-sectional studies have focused on the relationship between cardiorespiratory fitness, eye-based measures, and cognitive performance.^{93–95,108,113} This means that our current knowledge is relatively limited with respect to other fitness dimensions (e.g., motor fitness and muscular strength). Given that (a) there is growing evidence linking higher levels of muscular strength (e.g., operationalized via handgrip strength) to better cognitive performance, especially in older adults,^{178–180} and/or lower risk for developing neurological diseases (e.g., Alzheimer's disease)¹⁸¹ and (b) different fitness dimensions might influence cognitive performance and underlying neurobiological mechanisms in unique ways,^{7,98,182,183} investigating the effects of various fitness dimensions is likely to be a promising angle for future studies. Researchers might also consider utilizing the concept of 24-hour movement behaviors, which specifically quantifies physical activity, sedentary behavior, and sleep instead of assessing only the level of regular physical activity,^{184–187} to gain a more comprehensive understanding of the influence of movement behaviors on cognitive performance and to determine whether this association is driven by neurobiological processes that can be operationalized via eye-based measures.

We also saw that the majority of acute physical exercise studies used either continuous aerobic exercise on a treadmill^{93,125,132,135,137} or a stationary cycling ergometer,^{92,122–124,126–131,133,134} which is what previous reviews of acute exercise cognition studies also found.^{4,5} To achieve a deeper understanding of a possible dose–response relationship, we recommend that future studies evaluate the influence of different exercise characteristics (e.g., types of acute physical exercises) on cognitive performance and eye-based measures. Our systematic examination of the current state of the literature shows that the number of chronic physical exercise studies^{96,118–120} is considerably lower than the number of studies investigating the influence of an acute bout of physical exercise.^{92,93,122–136} For a

more nuanced understanding of acute and chronic effects of physical exercise, eye-based measures can be utilized in chronic physical exercise studies to elucidate possible mediators of the exercise–cognition interaction, which are now only partially understood.¹¹ As of now, there is only a single study in children showing physical training-induced changes in eye-based measures (i.e., retinal diameter) as positively correlated with changes in cognitive performance (i.e., executive functioning).⁹⁶

In summary, the findings of the current review are comparable to those of other reviews in the field of exercise–cognition^{3,6,8} in that they suggest further research is required to better understand the dose–response relationship (e.g., with respect to exercise and training variables) and the underlying neurobiological processes in cohorts with different age and/or health statuses. Furthermore, as the majority of the reviewed studies focused on healthy younger adults, future research should utilize more diverse study samples and consider moderators such as age, sex, health status, or educational level. In addition, as eye-derived measures are advantageous insofar as they can be used as proxies for different neurobiological processes, we recommend that researchers who aim to apply these measures in exercise–cognition science carefully choose the eye-derived measure that most closely reflects the neurobiological process of interest (e.g., retinal vessel analysis for studying cerebrovascular changes).

7. Conclusion

Overall, our systematic review provides evidence that acute and chronic physical exercise have a positive effect on oculomotor measures of executive functions (operationalized via antisaccade tasks). However, due to a limited number of studies utilizing gaze-fixation-based measures ($n = 2$), pupillometry ($n = 7$), spontaneous-eye blink rate ($n = 1$), and retinal vessel analysis ($n = 5$), no solid conclusions can be drawn. Still, the available studies suggest that physical training- or fitness-related changes in the cerebrovascular system (operationalized via changes in retinal vasculature) and the dopaminergic system (operationalized via resting-state spontaneous eye-blink rate) are positively associated with cognitive performance.

Given that (a) eye-based measures can be economically and non-invasively captured, (b) the current number of studies is relatively limited, and (c) eye-based measures can provide valuable insight into the neurobiological mechanisms driving the positive associations between physical activity and fitness and measures of cognitive performance, we hope the present systematic review will foster future applications for eye-based measures in the field of exercise–cognition science.

Authors' contributions

LZ, FH, and SL participated in conceptualization, methodology, validation, formal analysis, investigation, data curation, writing (original draft), visualization, and project administration; KK, NGM, MBP, MH, RK, HS, CHH, SA, BLA, BC, and AFK participated in writing (review and editing). All

authors have read and approved the final version of the manuscript, and agree with the order of presentation of the authors.

Competing interests

The authors declare that they have no competing interests.

Supplementary materials

Supplementary materials associated with this article can be found in the online version at doi:10.1016/j.jshs.2023.04.003.

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