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PII: S2095-2546(23)00042-X
DOI: https://doi.org/10.1016/j.jshs.2023.04.003
Reference: JSHS 861

To appear in: *Journal of Sport and Health Science*

Received date: 12 January 2023
Revised date: 7 March 2023
Accepted date: 16 March 2023

Please cite this article as: Liye Zou , Fabian Herold , Sebastian Ludyga , Keita Kamijo , Notger G. Müller , Matthew B. Pontifex , Matthew Heath , Ryuta Kuwamizu , Hideaki Soya , Charles H. Hillman , Soichi Ando , Brandon L. Alderman , Boris Cheval , Arthur F. Kramer , Look into my eyes: What can eye-based measures tell us about the relationship between physical activity and cognitive performance?, *Journal of Sport and Health Science* (2023), doi: https://doi.org/10.1016/j.jshs.2023.04.003

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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Running head: Relationship between PA and cognitive performance

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

Highlights

・There is insufficient evidence available to make solid conclusions concerning gaze-fixation-based measures.

・Pupillometric measures, as a proxy of the noradrenergic system, can explain the positive effect of acute exercise and cardiorespiratory fitness on cognitive performance is mixed.

・Physical training- or fitness-related changes of the cerebrovascular system (i.e., operationalized via changes in retinal vasculature) are, in general, positively associated with cognitive performance improvements.

・Acute and chronic physical exercises have a positive effect on oculomotor-based measures of executive function (i.e., operationalized via antisaccade tasks).

・ The positive association between cardiorespiratory fitness and cognitive performance is partly mediated by the dopaminergic system operationalized via the spontaneous eye-blink rate.

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 aims to address that gap in the literature.

Methods: To identify eligible studies, we searched 5 electronic databases on October 23rd 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 (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 and functional magnetic resonance imaging (MRI/fMRI), functional near-infrared spectroscopy (fNIRS) and event-related optical signals (EROS), 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.[28,29]). 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 hypothesis[36]). 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 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., including 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 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 status[66] 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-conditions[70] 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.[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.,[82,83]). 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 (BDNF))[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 neuromodulatory 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 hands- 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] 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 system[60] –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 material). 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 intensity[4] 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 (OSF; registration number: 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 material for more details), and the results of the systematic literature search were stored as supplementary material 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: **P**articipants, **I**ntervention, **C**omparisons, **O**utcomes, and **S**tudy 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:

(a) Population characteristics (e.g., age, gender, health status, and fitness level).
(b) Intervention-related characteristics (e.g., exercise intensity, duration, and type of exercise).
(c) Cognitive testing (e.g., tested cognitive domain, administration after exercise cessation or after acute exercise bouts).
(d) Methodological information (e.g., data processing procedures and data analysis).
(e) 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 **T**ool for the ass**E**ssment of **S**tudy quali**T**y and reporting in **EX**ercise (TESTEX scale)[105] for interventional studies and the critical appraisal tool from the Joanna Briggs Institute (JBI) 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 [107]). Regarding cross-sectional studies, the JBI critical appraisal 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, 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% 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 USA, 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 complaints[118] 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 years[112] (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 ergometer[133] 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 × age)),[132] (207 – (0.7 × age)),[136] (220 – age in years)[92,124,126,128,129,134]) or determined using maximal values obtained during a graded exercise test[93] 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 week[120] 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 individual[119] 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: ~100%,[118] 95%,[96] 88.4%,[119] and ~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: ~87%,[119] ~79%,[96] 77%, and 72% (for the two 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 with regular physical activity level.[111] However, Chandler and colleagues[94] 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. 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, one 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 one study, 35 adolescents were randomly allocated to either a 12-week exercise or active control intervention (i.e., social interaction).[96] 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 fitness[113] 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 activity[111] or the expertise/skill level in specific sports disciplines (e.g., amateuer athletes vs. elite athletes).[109,110,115] In particular, Zhou and colleagues[111] 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 controls[109] or had a shorter prosaccade reaction time[114] (see Table 1 for more details). In turn, Kokubu and colleagues[116] observed that volleyball players exhibited shorter dual-task prosaccade reaction times as compared to nonathletes.[116] In addition, Zhou[115] 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, antisaccade (but not pro-saccade) reaction time decreased from pretest to post-test,[118,119] although there was one 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, one 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 [141,142]) 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 JBI tool.[106] Most of these studies have a relatively low risk for bias concerning the majority of the items (see Table 2 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 Table 2). 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 exercise[93] 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 acute[136] 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 parameters[150] 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 performance[155] 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 hypothesis[36]) 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 activity[111] 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 activity[167] and sport-specific skills[168] 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 one 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 subjective[118] 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, MP, MH, RK, HS, CH, SA, BA, BC, and AK 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.

References

1. Caspersen CJ, Powell KE, Christenson GM. Physical activity, exercise, and physical fitness: Definitions and distinctions for health-related research. *Public Health Rep* 1985;**100**:126–31.
2. Ludyga S, Gerber M, Pühse U, Looser VN, Kamijo K. Systematic review and meta-analysis investigating moderators of long-term effects of exercise on cognition in healthy individuals. *Nat Hum Behav* 2020;**4**:603–12.
3. Hillman CH, Erickson KI, Kramer AF. Be smart, exercise your heart: Exercise effects on brain and cognition: Exercise effects on brain and cognition. *Nat Rev Neurosci* 2008;**9**:58–65.
4. Chang YK, Labban JD, Gapin JI, Etnier JL. The effects of acute exercise on cognitive performance: A meta-analysis. *Brain Res* 2012;**1453**:87–101.
5. Pontifex MB, McGowan AL, Chandler MC, et al. A primer on investigating the after effects of acute bouts of physical activity on cognition. *Psychol Sport Exerc* 2019;**40**:1–22. doi: 10.1016/j.psychsport.2018.08.015.
6. Erickson KI, Donofry SD, Sewell KR, Brown BM, Stillman CM. Cognitive aging and the promise of physical activity. *Annu Rev Clin Psychol* 2022;**18**:417–42.
7. Ludyga S, Gerber M, Kamijo K. Exercise types and working memory components during development. *Trends Cogn Sci* 2022;**26**:191–203.

8. Stillman CM, Esteban-Cornejo I, Brown B, Bender CM, Erickson KI. Effects of exercise on brain and cognition across age groups and health states. *Trends Neurosci* 2020;**43**:533–43.
9. Erickson KI, Hillman C, Stillman CM, et al. Physical activity, cognition, and brain outcomes: A review of the 2018 Physical Activity Guidelines. *Med Sci Sports Exerc* 2019;**51**:1242–51.
10. Ishihara T, Drollette ES, Ludyga S, Hillman CH, Kamijo K. The effects of acute aerobic exercise on executive function: A systematic review and meta-analysis of individual participant data. *Neurosci Biobehav Rev* 2021;**128**:258–69.
11. Stillman CM, Cohen J, Lehman ME, Erickson KI. Mediators of physical activity on neurocognitive function: A review at multiple levels of analysis. *Front Hum Neurosci* 2016;**10**:626. doi: 10.3389/fnhum.2016.00626.
12. Herold F, Törpel A, Schega L, Müller NG. Functional and/or structural brain changes in response to resistance exercises and resistance training lead to cognitive improvements - a systematic review. *Eur Rev Aging Phys Act* 2019;**16**:10. doi: 10.1186/s11556-019-0217-2.
13. Voss MW. The chronic exercise–cognition interaction: fMRI Research. In: McMorris T, editor. *Exercise-cognition interaction.* Cambridge, MA: Elsevier Academic Press; 2016.p.187–209.
14. Kao S-C, Cadenas-Sanchez C, Shigeta TT, et al. A systematic review of physical activity and cardiorespiratory fitness on P3b. *Psychophysiology* 2020;**57**:e13425. doi: 10.1111/psyp.13425.
15. Kamijo K. Physical Activity, Fitness, and Cognition. In: McMorris T, editor. *Exercise-cognition interaction.* Cambridge, MA: Elsevier Academic Press; 2016.p. 211–226.
16. Herold F, Wiegel P, Scholkmann F, Müller NG. Applications of functional near-infrared spectroscopy (fnirs) neuroimaging in exercise-cognition science: A systematic, methodology-focused review. *J Clin Med* 2018;**7**:466. doi: 10.3390/jcm7120466.
17. Salzman T, Dupuy O, Fraser SA. Effects of cardiorespiratory fitness on cerebral oxygenation in healthy adults: A systematic review. *Front Physiol* 2022;**13**:838450. doi: 10.3389/fphys.2022.838450.
18. Herold F, Aye N, Lehmann N, Taubert M, Müller NG. The contribution of functional magnetic resonance imaging to the understanding of the effects of acute physical exercise on cognition. *Brain Sci* 2020;**10**:175. doi: 10.3390/brainsci10030175.
19. Yu Q, Herold F, Becker B, et al. Cognitive benefits of exercise interventions: An fMRI activation likelihood estimation meta-analysis. *Brain Struct Funct* 2021;**226**:601–19.
20. Chen FT, Hopman RJ, Huang CJ, et al. The effect of exercise training on brain structure and function in older adults: A systematic review based on evidence from randomized control trials. *J Clin Med* 2020;**9**:914. doi: 10.3390/jcm9040914.
21. Aghjayan SL, Lesnovskaya A, Esteban-Cornejo I, Peven JC, Stillman CM, Erickson KI. Aerobic exercise, cardiorespiratory fitness, and the human hippocampus. *Hippocampus* 2021;**31**:817–44.
22. Erickson KI, Leckie RL, Weinstein AM. Physical activity, fitness, and gray matter volume. *Neurobiology of Aging* 2014;**35(Suppl. 2)**:S20-8. doi: 10.1016/j.neurobiolaging.2014.03.034.
23. Eckstein MK, Guerra-Carrillo B, Miller Singley AT, Bunge SA. Beyond eye gaze: What else can eyetracking reveal about cognition and cognitive development? *Dev Cogn Neurosci* 2017;**25**:69–91.

24. Krakauer JW, Ghazanfar AA, Gomez-Marin A, MacIver MA, Poeppel D. Neuroscience needs behavior: Correcting a reductionist bias. *Neuron* 2017;**93**:480–90.
25. Strauch C, Wang CA, Einhäuser W, van der Stigchel S, Naber M. Pupillometry as an integrated readout of distinct attentional networks. *Trends Neurosci* 2022;**45**:635–47.
26. Joshi S, Gold JI. Pupil size as a window on neural substrates of cognition. *Trends Cogn Sci* 2020;**24**:466–80.
27. Mathôt S. Pupillometry: Psychology, physiology, and function. *J Cogn* 2018;**1**:16. doi: 10.5334/joc.18.
28. Mahanama B, Jayawardana Y, Rengarajan S, et al. Eye movement and pupil measures: A review. *Front Comput Sci* 2022. doi: 10.3389/fcomp.2021.733531.
29. Hanssen H, Streese L, Vilser W. Retinal vessel diameters and function in cardiovascular risk and disease. *Prog Retin Eye Res* 2022;**91**:101095. doi: 10.1016/j.preteyeres.2022.101095.
30. McMorris T. The acute exercise-cognition interaction: From the catecholamines hypothesis to an interoception model. *Int J Psychophysiol* 2021;**170**:75–88.
31. McMorris T. Developing the catecholamines hypothesis for the acute exercise-cognition interaction in humans: Lessons from animal studies. *Physiol Behav* 2016;**165**:291–9.
32. McMorris T, Turner A, Hale BJ, Sproule J. Beyond the catecholamines hypothesis for an acute exercise–cognition interaction. In: McMorris T, editors. *Exercise-cognition interaction.* Cambridge, MA: Elsevier; 2016.p.65–103.
33. Spirduso WW. Physical fitness, aging, and psychomotor speed: A review. *J Gerontol* 1980;**35**:850–65.
34. Voss MW, Jain S. Getting fit to counteract cognitive aging: Evidence and future directions. *Physiology (Bethesda)* 2022. doi: 10.1152/physiol.00038.2021.
35. Dustman RE, Ruhling RO, Russell EM, et al. Aerobic exercise training and improved neuropsychological function of older individuals. *Neurobiol Aging* 1984;**5**:35–42.
36. Davenport MH, Hogan DB, Eskes GA, Longman RS, Poulin MJ. Cerebrovascular reserve: The link between fitness and cognitive function? *Exerc Sport Sci Rev* 2012;**40**:153–8.
37. Murphy PR, O'Connell RG, O'Sullivan M, Robertson IH, Balsters JH. Pupil diameter covaries with BOLD activity in human locus coeruleus. *Hum Brain Mapp* 2014;**35**:4140–54.
38. Schneider M, Hathway P, Leuchs L, Sämann PG, Czisch M, Spoormaker VI. Spontaneous pupil dilations during the resting state are associated with activation of the salience network. *NeuroImage* 2016;**139**:189–201.
39. DiNuzzo M, Mascali D, Moraschi M, Bussu G, Maugeri L, Mangini F, et al. Brain networks underlying eye's pupil dynamics. *Front Neurosci* 2019;**13**:965. doi: 10.3389/fnins.2019.00965.
40. Murphy PR, Robertson IH, Balsters JH, O'Connell RG. Pupillometry and P3 index the locus coeruleus-noradrenergic arousal function in humans. *Psychophysiology* 2011;**48**:1532–43.
41. Dahl MJ, Mather M, Sander MC, Werkle-Bergner M. Noradrenergic responsiveness supports selective attention across the adult lifespan. *J Neurosci* 2020;**40**:4372–90.
42. Hayat H, Regev N, Matosevich N, et al. Locus coeruleus norepinephrine activity mediates sensory-evoked awakenings from sleep. *Sci Adv* 2020;**6**:eaaz4232. doi: 10.1126/sciadv.aaz4232.
43. Privitera M, Ferrari KD, von Ziegler LM, et al. A complete pupillometry toolbox for real-time monitoring of locus coeruleus activity in rodents. *Nat Protoc* 2020;**15**:2301–20.

44. Zerbi V, Floriou-Servou A, Markicevic M, et al. Rapid reconfiguration of the functional connectome after chemogenetic locus coeruleus activation. *Neuron* 2019;**103**:702-718.e5.
45. Megemont M, McBurney-Lin J, Yang H. Pupil diameter is not an accurate real-time readout of locus coeruleus activity. *Elife* 2022;**11**:e70510. doi: 10.7554/eLife.70510.
46. Cazettes F, Reato D, Morais JP, Renart A, Mainen ZF. Phasic activation of dorsal raphe serotonergic neurons increases pupil size. *Curr Biol* 2021;**31**:192-197.e4.
47. Reimer J, McGinley MJ, Liu Y, et al. Pupil fluctuations track rapid changes in adrenergic and cholinergic activity in cortex. *Nat Commun* 2016;**7**:13289. doi: 10.1038/ncomms13289.
48. Sirois S, Brisson J. Pupillometry. *Wiley Interdiscip Rev Cogn Sci* 2014;**5**:679–92.
49. Hutton B. The cognitive control of saccadic eye movements. In: van der Heijden A, editor. *Attention in vision.* London, England: Psychology Press; 2004.p.257–90.
50. Hutton SB, Ettinger U. The antisaccade task as a research tool in psychopathology: A critical review. *Psychophysiol* 2006;**43**:302–13.
51. Munoz DP, Everling S. Look away: The anti-saccade task and the voluntary control of eye movement. *Nat Rev Neurosci* 2004;**5**:218–28.
52. Everling S, Fischer B. The antisaccade: A review of basic research and clinical studies. *Neuropsychologia* 1998;**36**:885–99.
53. Sparks DL. The brainstem control of saccadic eye movements. *Nat Rev Neurosci* 2002;**3**:952–64.
54. Funahashi S, Andreau JM. Prefrontal cortex and neural mechanisms of executive function. *J Physiol Paris* 2013;**107**:471–82.
55. Miller EK. The prefrontal cortex and cognitive control. *Nat Rev Neurosci* 2000;**1**:59–65.
56. Bäckman L, Farde L. Dopamine and cognitive functioning: Brain imaging findings in Huntington's disease and normal aging. *Scand J Psychol* 2001;**42**:287–96.
57. Bäckman L, Lindenberger U, Li SC, Nyberg L. Linking cognitive aging to alterations in dopamine neurotransmitter functioning: recent data and future avenues. *Neurosci Biobehav Rev* 2010;**34**:670–7.
58. Nieoullon A. Dopamine and the regulation of cognition and attention. *Prog Neurobiol* 2002;**67**:53–83.
59. Ott T, Nieder A. Dopamine and cognitive control in prefrontal cortex. *Trends Cogn Sci* 2019;**23**:213–34.
60. Jongkees BJ, Colzato LS. Spontaneous eye blink rate as predictor of dopamine-related cognitive function-A review. *Neurosci Biobehav Rev* 2016;**71**:58–82.
61. Dang LC, Samanez-Larkin GR, Castrellon JJ, Perkins SF, Cowan RL, Newhouse PA, et al. Spontaneous eye blink rate (EBR) is uncorrelated with Dopamine D2 receptor availability and unmodulated by dopamine agonism in healthy adults. *eNeuro* 2017. doi: 10.1523/ENEURO.0211-17.2017.
62. Sescousse G, Ligneul R, van Holst RJ, et al. Spontaneous eye blink rate and dopamine synthesis capacity: preliminary evidence for an absence of positive correlation. *Eur J Neurosci* 2018;**47**:1081–6.
63. Buitenweg JIV, Murre JMJ, Ridderinkhof KR. Spontaneous eye blinks predict executive functioning in seniors. *J Cogn Enhanc* 2021;**5**:468–79.
64. Paprocki R, Lenskiy A. What does eye-blink rate variability dynamics tell us about cognitive performance? *Front Hum Neurosci* 2017;**11**:620. doi: 10.3389/fnhum.2017.00620.

65. Zhang T, Di Mou, Wang C, et al. Dopamine and executive function: Increased spontaneous eye blink rates correlate with better set-shifting and inhibition, but poorer updating. *Int J Psychophysiol* 2015;**96**:155–61.
66. Ladas A, Frantzidis C, Bamidis P, Vivas AB. Eye blink rate as a biological marker of mild cognitive impairment. *Int J Psychophysiol* 2014;**93**:12–6.
67. Ortega J, Plaska CR, Gomes BA, Ellmore TM. Spontaneous eye blink rate during the working memory delay period predicts task accuracy. *Front Psychol* 2022;**13**:788231. doi: 10.3389/fpsyg.2022.788231.
68. Oh J, Han M, Peterson BS, Jeong J. Spontaneous eyeblinks are correlated with responses during the Stroop task. *PLoS One* 2012;**7**:e34871. doi: 10.1371/journal.pone.0034871.
69. Hornung T, Chan W-H, Müller R-A, Townsend J, Keehn B. Dopaminergic hypo-activity and reduced theta-band power in autism spectrum disorder: A resting-state EEG study. *Int J Psychophysiol* 2019;**146**:101–6.
70. Zhang T, Wang C, Tan F, Di Mou, Zheng L, Chen A. Different relationships between central dopamine system and sub-processes of inhibition: Spontaneous eye blink rate relates with N2 but not P3 in a Go/Nogo task. *Brain Cogn* 2016;**105**:95–103.
71. Zhang T, Yu L, Han X. The interaction effect between dopamine and task difficulty: Spontaneous eye blink rates diversely relate with Nogo-N2 across various task difficulties. *Int J Psychophysiol* 2020;**150**:1–10. doi: 10.1016/j.ijpsycho.2020.01.008.
72. Nakano T. The right angular gyrus controls spontaneous eyeblink rate: A combined structural MRI and TMS study. *Cortex* 2017;**88**:186–91.
73. Patton N, Aslam TM, MacGillivray T, et al. Retinal image analysis: concepts, applications and potential. *Prog Retin Eye Res* 2006;**25**:99–127.
74. van Dinther M, Voorter PH, Schram MT, et al. Retinal microvascular function is associated with the cerebral microcirculation as determined by intravoxel incoherent motion MRI. *Journal of the Neurological Sciences* 2022;**440**:120359. doi: 10.1016/j.jns.2022.120359.
75. Barnes JN, Corkery AT. Exercise improves vascular function, but does this translate to the brain? *Brain Plast* 2018;**4**:65–79.
76. de Carlo TE, Romano A, Waheed NK, Duker JS. A review of optical coherence tomography angiography (OCTA). *Int J Retina Vitreous* 2015;**1**:5. doi: 10.1186/s40942-015-0005-8.
77. Borrelli E, Sadda SR, Uji A, Querques G. Pearls and pitfalls of optical coherence tomography angiography imaging: A review. *Ophthalmol Ther* 2019;**8**:215–26.
78. Kashani AH, Chen CL, Gahm JK, et al. Optical coherence tomography angiography: A comprehensive review of current methods and clinical applications. *Prog Retin Eye Res* 2017;**60**:66–100.
79. Thayer JF, Mather M, Koenig J. Stress and aging: A neurovisceral integration perspective. *Psychophysiol* 2021;**58**:e13804. doi: 10.1111/psyp.13804.
80. Thayer JF. A neurovisceral integration model of heart rate variability. In: Stein J, editor. *Reference module in neuroscience and biobehavioral psychology:* Elsevier; 2017.
81. Thayer JF, Åhs F, Fredrikson M, Sollers 3rd JJ, Wager TD. A meta-analysis of heart rate variability and neuroimaging studies: Implications for heart rate variability as a marker of stress and health. *Neurosci Biobehav Rev* 2012;**36**:747–56.

82. Ludyga S, Pühse U, Lucchi S, Marti J, Gerber M. Immediate and sustained effects of intermittent exercise on inhibitory control and task-related heart rate variability in adolescents. *J Sci Med Sport* 2019;**22**:96–100.
83. Vrinceanu T, Lagacé-Lavoie G, Kaushal N, et al. Mind the rhythm: ECG QT dispersion and cognition in healthy older adults. *Front Psychol* 2020;**11**:566341. doi: 10.3389/fpsyg.2020.566341.
84. Walsh EI, Smith L, Northey J, Rattray B, Cherbuin N. Towards an understanding of the physical activity-BDNF-cognition triumvirate: A review of associations and dosage. *Ageing Res Rev* 2020;**60**:101044. doi: 10.1016/j.arr.2020.101044.
85. de Assis GG, de Almondes KM. Exercise-dependent BDNF as a modulatory factor for the executive processing of individuals in course of cognitive decline. A systematic review. *Front Psychol* 2017;**8**:584. doi: 10.3389/fpsyg.2017.00584.
86. Budde H, Voelcker-Rehage C, Pietrassyk-Kendziorra S, Machado S, Ribeiro P, Arafat AM. Steroid hormones in the saliva of adolescents after different exercise intensities and their influence on working memory in a school setting. *Psychoneuroendocrinology* 2010;**35**:382–91.
87. Niemann C, Wegner M, Voelcker-Rehage C, Holzweg M, Arafat AM, Budde H. Influence of acute and chronic physical activity on cognitive performance and saliva testosterone in preadolescent school children. *Mental Health Phy Act* 2013;**6**:197–204.
88. Yeung MK, Lee TL, Han YMY, Chan AS. Prefrontal activation and pupil dilation during n-back task performance: A combined fNIRS and pupillometry study. *Neuropsychologia* 2021:107954. doi: 10.1016/j.neuropsychologia.2021.107954.
89. Zhou X, Burg E, Kan A, Litovsky RY. Investigating effortful speech perception using fNIRS and pupillometry measures. *Curr Res Neurobiol* 2022;**3**:100052. doi: 10.1016/j.crneur.2022.100052.
90. Kaufman LD, Pratt J, Levine B, Black SE. Antisaccades: A probe into the dorsolateral prefrontal cortex in Alzheimer's disease. A critical review. *J Alzheimers Dis* 2010;**19**:781–93.
91. Kaufman LD, Pratt J, Levine B, Black SE. Executive deficits detected in mild Alzheimer's disease using the antisaccade task. *Brain Behav* 2012;**2**:15–21.
92. Ayala N, Heath M. Pupillometry reveals the role of arousal in a postexercise benefit to executive function. *Brain Sci* 2021;**11**:1048. doi: 10.3390/brainsci11081048.
93. Shigeta TT, Morris TP, Henry DH, et al. Acute exercise effects on inhibitory control and the pupillary response in young adults. *Int J Psychophysiol* 2021;**170**:218–28.
94. Chandler MC, McGowan AL, Brascamp JW, Pontifex MB. Phasic activity of the locus-coeruleus is not a mediator of the relationship between fitness and inhibition in college-aged adults. *Int J Psychophysiol* 2021;**165**:1–7.
95. Kuwamizu R, Suwabe K, Damrongthai C, et al. Spontaneous eye blink rate connects missing link between aerobic fitness and cognition. *Med Sci Sports Exerc* 2021;**53**:1425–33.
96. Ludyga S, Köchli S, Pühse U, Gerber M, Hanssen H. Effects of a school-based physical activity program on retinal microcirculation and cognitive function in adolescents. *J Sci Med Sport* 2019;**22**:672–6.
97. Ludyga S, Köchli S, Gerber M, Faude O, Zahner L, Hanssen H. Cardiovascular risk markers and cognitive performance in children. *J Pediatr* 2020;**224**:162-165.

98. Voelcker-Rehage C, Niemann C. Structural and functional brain changes related to different types of physical activity across the life span. *Neurosci Biobehav Rev* 2013;**37**:2268–95.
99. Northey JM, Cherbuin N, Pumpa KL, Smee DJ, Rattray B. Exercise interventions for cognitive function in adults older than 50: A systematic review with meta-analysis: A systematic review with meta-analysis. *Br J Sports Med* 2018;**52**:154–60.
100. Page MJ, Moher D, Bossuyt PM, et al. PRISMA 2020 explanation and elaboration: Updated guidance and exemplars for reporting systematic reviews. *BMJ* 2021;**372**:n160. doi: 10.1136/bmj.n160.
101. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *BMJ* 2021;**372**:n71.
102. Page MJ, McKenzie JE, Bossuyt PM, et al. Updating guidance for reporting systematic reviews: development of the PRISMA 2020 statement. *J Clin Epidemiol* 2021;**134**:103–12.
103. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA Statement. *J Clin Epidemiol* 2009;**62**:1006–12.
104. Hecksteden A, Faude O, Meyer T, Donath L. How to construct, conduct and analyze an exercise training study? *Front Physiol* 2018;**9**:1007. doi: 10.3389/fphys.2018.01007.
105. Smart NA, Waldron M, Ismail H, et al. Validation of a new tool for the assessment of study quality and reporting in exercise training studies: TESTEX. *Int J Evid Based Healthc* 2015;**13**:9–18.
106. Moola S, Munn Z, Sears K, et al. Conducting systematic reviews of association (etiology): The Joanna Briggs Institute's approach. *Int J Evid Based Healthc* 2015;13:163-9.
107. Büttner F, Winters M, Delahunt E, et al. Identifying the "incredible"! Part 2: Spot the difference - a rigorous risk of bias assessment can alter the main findings of a systematic review. *Br J Sports Med* 2020;**54**:801–8.
108. McGowan AL, Chandler MC, Pontifex MB. Aerobic fitness relates to superior exact and approximate arithmetic processing in college-aged adults. *Trends Neurosci Educ* 2021;**23**:100154. doi: 10.1016/j.tine.2021.100154.
109. Fujiwara K, Kiyota N, Maekawa M, Kunita K, Kiyota T, Maeda K. Saccades and prefrontal hemodynamics in basketball players. *Int J Sports Med* 2009;**30**:647–51.
110. Yilmaz A, Polat M. Prosaccadic and antisaccadic performance of the athletes in different types of sports. *Biomed Res* 2018;**29**:539-43.
111. Zhou J, Zhuang W. Physically active undergraduates perform better on executive-related oculomotor control: Evidence from the antisaccade task and pupillometry. *Psych J* 2023;**12**:17–24.
112. Roeh A, Schoenfeld J, Raab R, et al. Effects of marathon running on cognition and retinal vascularization: A longitudinal observational study. *Med Sci Sports Exerc* 2021;**53**:2207–14.
113. Fang M, Strand K, Zhang J, et al. Retinal vessel density correlates with cognitive function in older adults. *Experimental Gerontology* 2021;**152**:111433. doi: 10.1016/j.exger.2021.111433.
114. Kunita K, Fujiwara K. Influence of sports experience on distribution of pro-saccade reaction time under gap condition. *J Physiol Anthropol* 2022;**41**:4. doi: 10.1186/s40101-022-00277-1.

115. Zhou J. Differences on prosaccade task in skilled and less skilled female adolescent soccer players. *Front Psychol* 2021;**12**:711420. doi: 10.3389/fpsyg.2021.711420.

116. Kokubu M. Interference effects between saccadic and key-press reaction times of volleyball players and nonathletes. *Percept Mot Skills* 2006;**103**:709-16.

117. Cheval B, Miller MW, Orsholits D, Berry T, Sander D, Boisgontier MP. Physically active individuals look for more: An eye-tracking study of attentional bias. *Psychophysiol* 2020;**57**:e13582. doi: 10.1111/psyp.13582.

118. Heath M, Shellington E, Titheridge S, Gill DP, Petrella RJ. A 24-week multi-modality exercise program improves executive control in older adults with a self-reported cognitive complaint: Evidence from the antisaccade task. *J Alzheimers Dis* 2017;**56**:167–83.

119. Heath M, Weiler J, Gregory MA, Gill DP, Petrella RJ. A six-month cognitive-motor and aerobic exercise program improves executive function in persons with an objective cognitive impairment: A pilot investigation using the antisaccade task. *J Alzheimers Dis* 2016;**54**:923–31.

120. Fang M, Strand K, Zhang J, Totillo M, Chen Q, Signorile JF, et al. Characterization of retinal microvasculature and its relations to cognitive function in older people after circuit resistance training. *Exp Gerontol* 2020;**142**:111114. doi: 10.1016/j.exger.2020.111114.

121. Shellington EM, Reichert SM, Heath M, Gill DP, Shigematsu R, Petrella RJ. Results from a feasibility study of square-stepping exercise in older adults with type 2 diabetes and self-reported cognitive complaints to improve global cognitive functioning. *Can J Diabetes* 2018;**42**:603-612.

122. Dirk KL, Belfry GR, Heath M. Exercise and executive function during follicular and luteal menstrual cycle phases. *Med Sci Sports Exerc* 2020;**52**:919–27.

123. Heath M, Petrella A, Blazevic J, Lim D, Pelletier A, Belfry GR. A post-exercise facilitation of executive function is independent of aerobically supported metabolic costs. *Neuropsychologia* 2018;**120**:65–74.

124. Heath M, Shukla D. A single bout of aerobic exercise provides an immediate "boost" to cognitive flexibility. *Front Psychol* 2020;**11**:1106. doi: 10.3389/fpsyg.2020.01106.

125. Petrella AFM, Belfry G, Heath M. Older adults elicit a single-bout post-exercise executive benefit across a continuum of aerobically supported metabolic intensities. *Brain Res* 2019;**1712**:197–206.

126. Samani A, Heath M. Executive-related oculomotor control is improved following a 10-min single-bout of aerobic exercise: Evidence from the antisaccade task. *Neuropsychologia* 2018;**108**:73–81.

127. Shirzad M, Tari B, Dalton C, van Riesen J, Marsala MJ, Heath M. Passive exercise increases cerebral blood flow velocity and supports a postexercise executive function benefit. *Psychophysiology* 2022;**59**:e14132. doi: 10.1111/psyp.14132.

128. Shukla D, Al-Shamil Z, Belfry G, Heath M. A single bout of moderate intensity exercise improves cognitive flexibility: Evidence from task-switching. *Exp Brain Res* 2020;**238**:2333–46.

129. Shukla D, Heath M. A single bout of exercise provides a persistent benefit to cognitive flexibility. *Res Q Exerc Sport* 2022;**93**:516–27.

130. Tari B, Shirzad M, Behboodpour N, Belfry GR, Heath M. Exercise intensity-specific changes to cerebral blood velocity do not modulate a postexercise executive function benefit. *Neuropsychologia* 2021;**161**:108018. doi: 10.1016/j.neuropsychologia.2021.108018.

131. Tari B, Vanhie JJ, Belfry GR, Shoemaker JK, Heath M. Increased cerebral blood flow supports a single-bout postexercise benefit to executive function: Evidence from hypercapnia. *J Neurophysiol* 2020;**124**:930–40.

132. McGowan AL, Chandler MC, Brascamp JW, Pontifex MB. Pupillometric indices of locus-coeruleus activation are not modulated following single bouts of exercise. *Int J Psychophysiol* 2019;**140**:41–52.

133. Tsai CL, Chang YC, Pan CY, Wang TC, Ukropec J, Ukropcová B. Acute effects of different exercise intensities on executive function and oculomotor performance in middle-aged and older adults: Moderate-intensity continuous exercise *vs*. high-intensity interval exercise. *Front Aging Neurosci* 2021;**13**:743479. doi: 10.3389/fnagi.2021.743479.

134. Zhou J, Wang L. Differences in the effects of reading and aerobic exercise interventions on inhibitory control of college students with mobile phone addiction. *Front Psychiatry* 2022;**13**:797780. doi: 10.3389/fpsyt.2022.797780.

135. Thom NJ, Campbell MJ, Reyes C, Herring MP. Effect of acute aerobic exercise on ocular measures of attention to emotionally expressive faces. *Int J Behav Med* 2021;**28**:372–81.

136. Solianik R, Bružas V, Mockus P, Vadopalas K, Streckis V. Acute effects of high-intensity interval training on cognition and retinal microcirculation in experienced amateur boxers. *J Sports Med Phys Fitness* 2021;**61**:867–73.

137. Shaw BS, Jan Breukelman G, Millard L, Shaw I. Effect of a prolonged maximal bout of exercise on visual performance. *Asian J Sports Med* 2022;**13**:e119406. doi: 10.5812/asjsm.119406.

138. Hawley-Hague H, Horne M, Skelton DA, Todd C. Review of how we should define (and measure) adherence in studies examining older adults' participation in exercise classes. *BMJ Open* 2016;**6**(6):e011560. doi: 10.1136/bmjopen-2016-011560.

139. Rivera-Torres S, Fahey TD, Rivera MA. Adherence to exercise programs in older adults: Informative report. *Gerontol Geriatr Med* 2019;5:2333721418823604. doi: 10.1177/2333721418823604.

140. Pontifex MB, Gwizdala KL, Weng TB, Zhu DC, Voss MW. Cerebral blood flow is not modulated following acute aerobic exercise in preadolescent children. *Int J Psychophysiol* 2018;**134**:44–51.

141. Curtin A, Ayaz H. Neural efficiency metrics in neuroergonomics. In: Ayaz H, editors. *Neuroergonomics*. London, England: Elsevier; 2019.p.133–140.

142. Curtin A, Ayaz H, Tang Y, Sun J, Wang J, Tong S. Enhancing neural efficiency of cognitive processing speed via training and neurostimulation: An fNIRS and TMS study. *Neuroimage* 2019;**198**:73–82.

143. Ludyga S, Ishihara T, Kamijo K. The nervous system as a pathway for exercise to improve social cognition. *Exerc Sport Sci Rev* 2022;**50**:203–12.

144. Robison MK, Coyne JT, Sibley C, Brown NL, Neilson B, Foroughi C. An examination of relations between baseline pupil measures and cognitive abilities. *Psychophysiol* 2022;**59**:e14124. doi: 10.1111/psyp.14124.

145. Tsukahara JS, Engle RW. Is baseline pupil size related to cognitive ability? Yes (under proper lighting conditions). *Cognition* 2021;**211**:104643. doi: 10.1016/j.cognition.2021.104643.

146. Tsukahara JS, Harrison TL, Engle RW. The relationship between baseline pupil size and intelligence. *Cogn Psychol* 2016;**91**:109–23.

147. Unsworth N, Miller AL, Robison MK. Is working memory capacity related to baseline pupil diameter? *Psychon Bull Rev* 2021;**28**:228–37.

148. Kuwamizu R, Yamazaki Y, Aoike N, Ochi G, Suwabe K, Soya H. Pupil-linked arousal with very light exercise: Pattern of pupil dilation during graded exercise. *J Physiol Sci* 2022;**72**:23. doi: 10.1186/s12576-022-00849-x.

149. Ishigaki H, Miyao M, Ishihara S. Change of pupil size as a function of exercise. *J Hum Ergol (Tokyo)* 1991;**20**:61–6.

150. Streese L, Guerini C, Bühlmayer L, et al. Physical activity and exercise improve retinal microvascular health as a biomarker of cardiovascular risk: A systematic review. *Atherosclerosis* 2020;**315**:33–42.

151. Luyten LJ, Dockx Y, Madhloum N, et al. Association of retinal microvascular characteristics with short-term memory performance in children aged 4 to 5 years. *JAMA Netw Open* 2020;**3**:e2011537. doi: 10.1001/jamanetworkopen.2020.11537.

152. Provost EB, Nawrot TS, Int Panis L, Standaert A, Saenen ND, de Boever P. Denser retinal microvascular network is inversely associated with behavioral outcomes and sustained attention in children. *Front Neurol* 2021;**12**:547033. doi: 10.3389/fneur.2021.547033.

153. Wei FF, Raaijmakers A, Zhang ZY, et al. Association between cognition and the retinal microvasculature in 11-year old children born preterm or at term. *Early Hum Dev* 2018;**118**:1–7. doi: 10.1016/j.earlhumdev.2018.01.018.

154. Appaji A, Nagendra B, Chako DM, et al. Relation between retinal vascular abnormalities and working memory impairment in patients with schizophrenia and bipolar disorder. *Asian J Psychiatr* 2020;**49**:101942. doi: 10.1016/j.ajp.2020.101942.

155. Shalev I, Moffitt TE, Wong TY, et al. Retinal vessel caliber and lifelong neuropsychological functioning: Retinal imaging as an investigative tool for cognitive epidemiology. *Psychol Sci* 2013;**24**:1198–207.

156. Cheung CY, Wong WLE, Hilal S, et al. Deep-learning retinal vessel calibre measurements and risk of cognitive decline and dementia. *Brain Commun* 2022;**4**:fcac212. doi: 10.1093/braincomms/fcac212.

157. Cheung CY, Ong S, Ikram MK, et al. Retinal vascular fractal dimension is associated with cognitive dysfunction. *J Stroke Cerebrovasc Dis* 2014;**23**:43–50.

158. Liew G, Mitchell P, Wong TY, et al. Retinal microvascular signs and cognitive impairment. *J Am Geriatri Soc* 2009;**57**:1892–6.

159. Ong YT, Hilal S, Cheung CY, et al. Retinal vascular fractals and cognitive impairment. *Dement Geriatr Cogn Dis Extra* 2014;**4**:305–13.

160. Jong FJ de, Schrijvers EMC, Ikram MK, et al. Retinal vascular caliber and risk of dementia: The Rotterdam study. *Neurology* 2011;**76**:816–21.

161. Cheung CY, Ong YT, Ikram MK, et al. Microvascular network alterations in the retina of patients with Alzheimer's disease. *Alzheimers Dement* 2014;**10**:135–42.

162. Jiang H, Wei Y, Shi Y, et al. Altered macular microvasculature in mild cognitive impairment and Alzheimer's Disease. *J Neuroophthalmol* 2018;**38**:292–8.

163. Williams MA, McGowan AJ, Cardwell CR, et al. Retinal microvascular network attenuation in Alzheimer's disease. *Alzheimers Dement (Amst)* 2015;**1**:229–35.

164. McGrory S, Ballerini L, Okely JA, et al. Retinal microvascular features and cognitive change in the Lothian-Birth Cohort 1936. *Alzheimers Dement (Amst)* 2019;**11**:500–9.

165. Taylor AM, MacGillivray TJ, Henderson RD, et al. Retinal vascular fractal dimension, childhood IQ, and cognitive ability in old age: The Lothian Birth Cohort Study 1936. *PLoS One* 2015;**10**:e0121119. doi: 10.1371/journal.pone.0121119.

166. O'Neill RA, Maxwell AP, Paterson EN, et al. Retinal microvascular parameters are not significantly associated with mild cognitive impairment in the Northern Ireland Cohort for the Longitudinal Study of Ageing. *BMC Neurol* 2021;**21**:112. doi: 10.1186/s12883-021-02137-4.

167. Cox EP, O'Dwyer N, Cook R, et al. Relationship between physical activity and cognitive function in apparently healthy young to middle-aged adults: A systematic review. *J Sci Med Sport* 2016;**19**:616–28.

168. Logan NE, Henry DA, Hillman CH, Kramer AF. Trained athletes and cognitive function: A systematic review and meta-analysis. *Int J Sport Exerc Psychol* 2022. doi:10.1080/1612197X.2022.2084764.

169. Ludyga S, Gerber M, Brand S, Holsboer-Trachsler E, Pühse U. Acute effects of moderate aerobic exercise on specific aspects of executive function in different age and fitness groups: A meta-analysis. *Psychophysiol* 2016;**53**:1611–26.

170. Bherer L, Erickson KI, Liu-Ambrose T. A review of the effects of physical activity and exercise on cognitive and brain functions in older adults. *J Aging Res* 2013;**2013**:657508. doi: 10.1155/2013/657508.

171. Dang LC, Castrellon JJ, Perkins SF, et al. Reduced effects of age on dopamine D2 receptor levels in physically active adults. *NeuroImage* 2017;**148**:123–9.

172. Shih C-H, Moore K, Browner N, Sklerov M, Dayan E. Physical activity mediates the association between striatal dopamine transporter availability and cognition in Parkinson's disease. *Parkinsonism Relat Disord* 2019;**62**:68–72.

173. Köhncke Y, Papenberg G, Jonasson L, et al. Self-rated intensity of habitual physical activities is positively associated with dopamine D2/3 receptor availability and cognition. *Neuroimage* 2018;**181**:605–16.

174. Jonasson LS, Nyberg L, Axelsson J, Kramer AF, Riklund K, Boraxbekk CJ. Higher striatal D2-receptor availability in aerobically fit older adults but non-selective intervention effects after aerobic versus resistance training. *NeuroImage* 2019;**202**:116044. doi: 10.1016/j.neuroimage.2019.116044.

175. Carter BT, Luke SG. Best practices in eye tracking research. *Int J Psychophysiol* 2020;**155**:49–62.

176. Laeng B, Alnaes D. Pupillometry. In: Klein C, Ettinger U, editors. *Eye Movement Research*. Cham: Springer International Publishing; 2019.p.449–502.

177. Steinhauer SR, Bradley MM, Siegle GJ, Roecklein KA, Dix A. Publication guidelines and recommendations for pupillary measurement in psychophysiological studies. *Psychophysiology* 2022;**59**:e14035. doi: 10.1111/psyp.14035.

178. Fritz NE, McCarthy CJ, Adamo DE. Handgrip strength as a means of monitoring progression of cognitive decline–A scoping review. *Ageing Res Rev* 2017;**35**:112–23.

179. Shaughnessy KA, Hackney KJ, Clark BC, et al. A narrative review of handgrip strength and cognitive functioning: Bringing a new characteristic to muscle memory. *J Alzheimers Dis* 2020;**73**:1265–78.

180. Zammit AR, Piccinin AM, Duggan EC, et al. A coordinated multi-study analysis of the longitudinal association between handgrip strength and cognitive function in older adults. *J Gerontol B Psychol Sci Soc Sci* 2021;**76**:229–41.

181. Cui M, Zhang S, Liu Y, Gang X, Wang G. Grip strength and the risk of cognitive decline and dementia: A systematic review and meta-analysis of longitudinal cohort studies. *Front Aging Neurosci* 2021;**13**:625551. doi: 10.3389/fnagi.2021.625551.

182. Voelcker-Rehage C, Godde B, Staudinger UM. Physical and motor fitness are both related to cognition in old age. *Eur J Neurosci* 2010;**31**:167–76.

183. Voss MW, Nagamatsu LS, Liu-Ambrose T, Kramer AF. Exercise, brain, and cognition across the life span. *J Appl Physiol (1985)* 2011;**111**:1505–13.

184. Tremblay MS, Colley RC, Saunders TJ, Healy GN, Owen N. Physiological and health implications of a sedentary lifestyle. *Appl Physiol Nutr Metab* 2010;**35**:725–40.

185. Chaput JP, Carson V, Gray CE, Tremblay MS. Importance of all movement behaviors in a 24 hour period for overall health. *Int J Environ Res Public Health* 2014;**11**:12575–81.

186. Rollo S, Antsygina O, Tremblay MS. The whole day matters: Understanding 24-hour movement guideline adherence and relationships with health indicators across the lifespan. *J Sport Health Sci* 2020;**9**:493–510.

187. Pedisic Z, Dumuid D, Olds TS. Integrating sleep, sedentary behaviour, and physical activity research in the emerging field of time-use epidemiology: Definitions, concepts, statistical methods, theoretical framework, and future directions. *Kinesiology* 2017;**49**:252–69.

188. Garber CE, Blissmer B, Deschenes MR, et al. American College of Sports Medicine position stand. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: guidance for prescribing exercise. *Med Sci Sports Exerc* 2011;**43**:1334–59.

189. Zhu W. Sadly, the earth is still round ($p < 0.05$). *J Sport Health Sci*2012;**1**:9–11.

190. Zhu W. $p < 0.05$, < 0.01, < 0.001, < 0.0001, < 0.00001, < 0.000001, or < 0.0000001 … *J Sport Health Sci* 2016;**5**:77–9.

191. Coe BC, Munoz DP. Mechanisms of saccade suppression revealed in the anti-saccade task. *Philos Trans R Soc Lond B Biol Sci* 2017;**372**:20160192. doi: 10.1098/rstb.2016.0192.

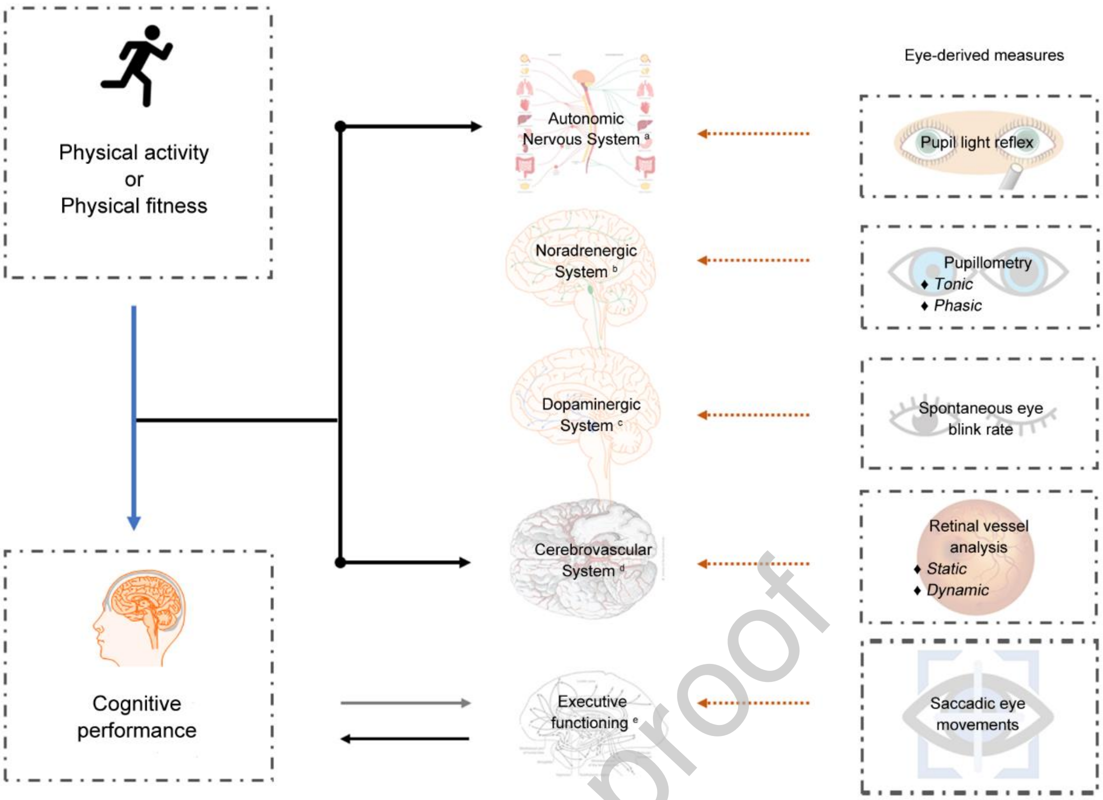


Fig. 1: Schematic overview of selected eye-based measures and their associations with distinct neurobiological mechanisms.

[a] such as pupil light reflex; [26,27] [b] based on the findings of, [5,27] although recent observations imply that pupil diameter is a result of a rather complex interplay of different neural systems[25] (e.g., including the cholinergic system in the basal forebrain[47]); [c] based on the findings of; [73,96] [d] based on the findings of; [60] [e] based on the findings of.[51,191]

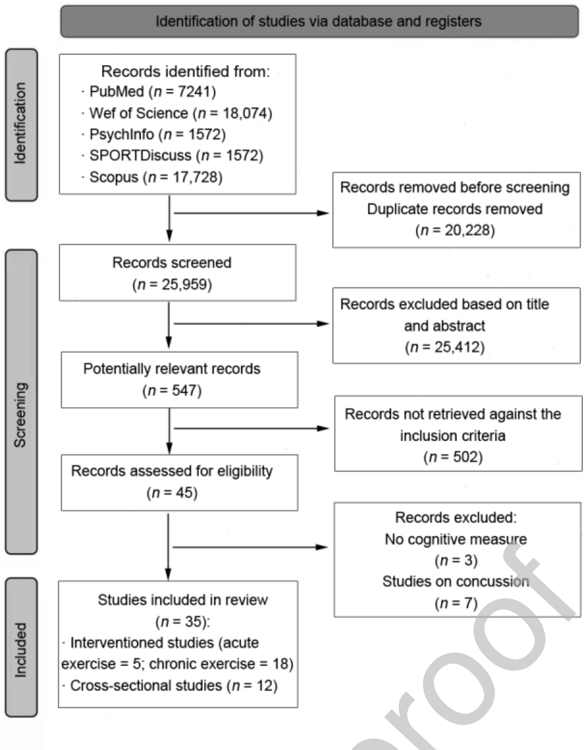


Fig. 2: Flow diagram of data search, screening, and assessment.

Table 1. Overview of study characteristics (i.e., study design and sample characteristics, characteristics of the physical intervention, and cognitive measures and main findings).

First author	Study design and sample characteristics	Characteristics of the physical interventions	Cognitive testing and main findings
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	(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 (3.1) 42.3 ± 9.0 mL/kg/min (3.2) n.r. / n.r. / n.r.	(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 and CRF (adjusted for age, sex, race, body fat, and task congruency)
McGowan et al. (2019) [132]	(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) 46.5 ± 8.7 mL/kg/min (3.2) n.a./n.a. / 24.6 ± 7.7 kg/m^2	(3) Moderate intensity (65%–75% of predicted HR_{max}) in EX/walking at 0.5 mph in active CC (4) 20 min	(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 = 138 (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 (4) 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)
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 m) ▪ 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 (3.1) 41.7 ± 3.8 l kg/min (recreationally active) (3.2) n.r./58.0 ± 7.5 kg/n.r.	(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
Fujiwara et al. (2009) [109]	(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)	(1) n.a. (2) n.a.	(1) Pro- and anti-saccade 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

	▪ 20.3 ± 1.5 years (3.1) n.r. (3.2) n.r.		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 $VO_{2\ peak}$), very heavy (at 50% of the difference between their LT and $VO_{2\ peak}$), and light intensity in the warm-up (20W) * (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-posttest 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/m^2; M4: 28.0 ± 3.8 kg/m^2	(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 anti-saccade 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/m^2; HC: 28.3 ± 3.2 kg/m^2	(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) ▪ 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 hours 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 ± 4.7kg; non-athletes: 59.3 ± 2.9 kg	(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 *vs*. nonathletes in the dual-task condition ▪ (-) No statistically significant differences between groups concerning saccadic measures
Kunita et al. (2022) [114]	(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 ± n.r. years ▪ Basketball: 20.8 ± n.r. years ▪ Table tennis: 20.4 ± n.r. years (3.1) n.r. (3.2) n.r	(1) n.a. (2) n.a.	(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/m^2	(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 anti-saccade 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]	(1) 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. (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) Low intensity* (2) 60 min (including 5–10-min warm-up + 5–10-min cool-down)	(1) 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
Shirzad et al. (2012) [127]	(1) RCT with within-subject design and pretest/post-test comparisons (2) Passive exercise CC (i.e., mechanically driven cycle ergometer) & 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 watts) * (2) 20 min (+ 2 min warm-up and cool-down, respectively)	(1) Pro- and anti-saccade task (2)▪↓ antisaccade (but not prosaccade) RT from pre-test 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	(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)

	points/CG: 68.0 ± 24.0 points) (3.2) n.r./n.r./n.r.		
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 (students) ▪ *n* = 16 (5 females/11 males) ▪ 22.8 ± 1.6 years (3.1) 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 Watt) * (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 (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	(1) Vigorous intensity in HIIE (70%–75% of HRR in working bout / 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	(1) Pro- and anti-saccade task (2) ▪ ↓ RT in antisaccade (but not 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

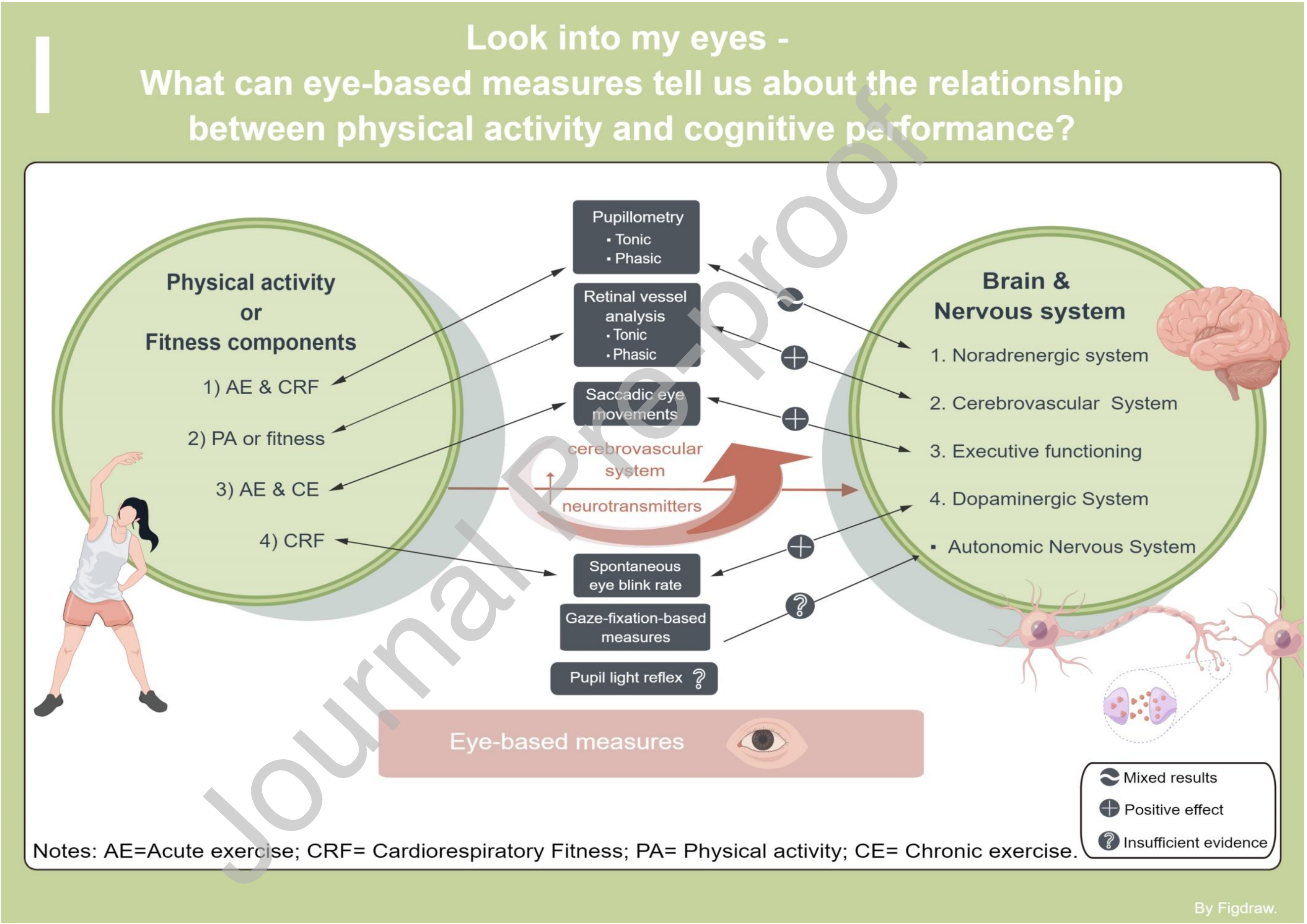
Yilmaz et al. (2018) [110]	(1) Cross-sectional study (2) Comparison of athletes with different sports backgrounds (tennis *vs*. volleyball *vs*. basketball *vs*. swimmers *vs*. CG) (4) Healthy younger adults ▪ n = 50 (50 males) ▪ Tennis: 21.9 ± 1.4 years ▪ Volleyball: 21.6 ± 1.6 years ▪ Basketball: 22.1 ± 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 anti-saccade 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; CG: 1060.5 ± 1636.4 (3.2) EX: 163.0 ± 7.7; CG: 165.4 ± 8.2/51.8 ± 6.5 kg; CG: 68.9 ± 24.9/EX: 19.4 ± 1.4; CG: 24.9 ± 2.9	(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 (23 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. (2020) [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) ▪ ↑ correlation between CRF and Stroop interference performance is mediated by resting-state spontaneous eye blink rate (adjusted for age and BMI)

Notes: ↑ 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; MICE = moderate-intensity continuous exercise; MVPA = moderate-to-vigorous physical activity; n.a. = not applicable; n.r. = not reported; OCI = objective cognitive impairment; PA = physically active; $PETCO_2$ = 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 YMCA; VO_{2pea} = peak oxygen uptake during a graded exercise test.

Graphic abstract


Look into my eyes -
What can eye-based measures tell us about the relationship between physical activity and cognitive performance?
Physical activity
or
Fitness components
1) AE & CRF
2) PA or fitness
3) AE & CE
4) CRF
Pupillometry
Tonic
Phasic
Retinal vessel analysis
Tonic
Phasic
Saccadic eye movements
cerebrovascular system
neurotransmitters
Spontaneous eye blink rate
Gaze-fixation-based measures
Pupil light reflex
Eye-based measures
Brain &
Nervous system
1. Noradrenergic system
2. Cerebrovascular System
3. Executive functioning
4. Dopaminergic System
Autonomic Nervous System
Mixed results
Positive effect
Insufficient evidence
Notes: AE=Acute exercise; CRF= Cardiorespiratory Fitness; PA= Physical activity; CE= Chronic exercise.
By Figdraw.