

1 Measuring the effect of aerobic exercise in the human eye: a scoping
2 review protocol
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Abstract

Background

Exercise improves blood flow in the retina and is protective in retinal disease. Recent advances have transformed retinal optical imaging, and started to change our understanding of the pathogenesis of retinal disease. The aim of the scoping review is to map current methods used to measure the effect of aerobic exercise in the human eye.

Methods

We will use a three-step search strategy to identify relevant studies. The search strategy will be developed by an academic librarian in collaboration with the review authors. We will include studies involving humans, published after 2000 in English, German and Scandinavian languages, using experimental and epidemiological study designs, including randomized controlled trials, non-randomized controlled trials, quasi-experimental studies, before and after studies, prospective and retrospective cohort studies, case-control studies, and analytical cross-sectional studies. A two-step approach will complete the screening and selection of studies based on predefined inclusion and exclusion criteria. Two independent reviewers will screen titles and abstracts to identify potential eligible studies, and then two pairs of reviewers will screen the full text for inclusion. In case of disagreement, the reviewers will discuss to reach consensus. If they fail to reach consensus, a third reviewer will make the decision. A PRISMA flow chart will document the process and selection. We will extract, collate, and summarize the data to provide a narrative map of measurement methods of the effect of aerobic exercise in the eye using descriptive thematic analysis, and provide a critical appraisal of the included studies. Reporting will follow PRISMA guidelines, and text, tables, and bubble diagrams will present the results. The discussion will address potential knowledge gaps.

Discussion

Ethical approval of review of published scientific work is not required. We will ensure transparency and rigorousness of the research by publication of the protocol and findings.

Systematic review registration

This protocol is registered in Figshare, doi: 10.23642/usn.14535306

Keywords:

Review, Aerobic Exercise, Eye, Retina, Physiology, Investigative Technique

Background

The benefit of a physical active lifestyle in prevention of chronic diseases and premature death are well documented.(1,2) The preventive effect of physical activity is related to physiological adaptations, including improvement in cardiorespiratory fitness, blood glucose control, blood lipid profile, body composition, inflammation, and blood pressure.(3,4) Further, physical activity also seem to have impact on eye health. Exercise adapts the normal blood flow in the retina and choroid, likely improving retinal nourishment and preventing retinal disease.(5) Age-related macular degeneration, glaucoma and diabetic retinopathy are among the five most common causes of visual impairment.(6) Higher levels of physical activity are associated with lower occurrence of diabetic retinopathy, and has a protective effect on age-related macular degeneration and glaucoma. While the World Health Organization has a global agenda to reduce the burden of eye disease and vision loss,(7) exercise as a strategy to prevent and reduce vision impairment is overlooked.

The eye is a window to health and disease. A recent review highlights the effect of exercise on retinal microvascular health through life, and the retinal vessel analysis as a monitoring tool.(8) However, recent advances has transformed retinal optical imaging, as well as started to change our understanding of the pathogenesis of retinal disease and play an increasing role in the early diagnosis and management.(9) The new imaging modalities include optical coherence tomography (OCT), optical coherence tomography angiography (OCTA), photoacoustic microscopy (PAM), adaptive optics (AO), scanning laser ophthalmoscopy (SLO), fundus autofluorescence (FAF), and molecular imaging. OCT and OCTA are commercially available and provide non-invasive capture of retinal structures and microvasculature. OCTA also provides vascular maps visualizing and quantifying retinal perfusion and foveal avascular zone.(10) At present, there are no clinical approved systems for PAM in the eye, and reported results are from in vivo or animal studies. However, PAM can provide estimates of oxygen saturation of haemoglobin (sO₂) and retinal metabolic rate of oxygen (rMRO₂), and in combination with SD-OCT both sO₂ and blood flow rate can be measured and advance our understanding of eye diseases like diabetic retinopathy and glaucoma.(9) AO allows in-vivo imaging at cellular level and SLO enhances imaging contrast. FAF map fluorophosphores in the retina and provides information on the metabolic state and the general health of the retinal pigment epithelium and photoreceptors. Whereas molecular imaging aims to visualize molecular process and functional changes. Hence, there are numerous new potential options to measure effect of aerobic exercise in the eye using commercial and experimental methods. A preliminary search for existing scoping reviews and systematic reviews in PubMed and Cochrane Database of Systematic Reviews (22.02.2021) did not identify any published reviews on methods of measuring the effect of aerobic exercise in the eye. The objective of this scoping review is to map current methods used to measure the effect of aerobic exercise in the human eye.

Methods

The scoping review will follow the JBI Manual for Evidence Synthesis for Scoping review,(11) and the Preferred Reporting Items for Systematic Reviews and Meta-Analysis extension for Scoping Reviews (PRISMA-ScR).(12) The scoping review is registered in the online open access repository Figshare.

Identifying the research question

The main aim of the scoping review is to map measurement methods of the effect of aerobic exercise in the eye, in specific the retina and choroid. We will identify theoretical foundations of the effect of aerobic exercise (physiological adaptation and effect on pathophysiology), main concepts of

measurements (outcome measures), sources of measurements (methods of examinations), as well as knowledge gaps related to application of the eye as an outcome measure of aerobic exercise in research and clinical practice. The scoping review questions are:

1. *“What physiological adaptations to aerobic exercise is observed in the eye?”*
2. *“What impact does aerobic exercise have on pathophysiology in eye?”*
3. *“What eye structures are used as outcome measures for effect of aerobic exercise?”*
4. *“What methods of examination are used to assess the effect of aerobic exercise in the eye?”*
5. *“What are the knowledge gaps of measuring the effect of aerobic exercise in the eye?”*

Identifying relevant studies

We will use a three-step search strategy to identify relevant studies. First, we will perform literature searches in the databases Medline and Embase including studies involving humans, published after 2000 in English, German and Scandinavian languages. The search strategy will be adapted to each database by an academic librarian in collaboration with the researchers involved in the scoping review. The search will consist of controlled keywords (Thesaurus / Medical subject headings (MESH) and text words (keywords)) for “training AND eye health AND measurement methods”, full search terms are provided in Supplementary File 1. Second, we will analyse the text words contained in the title and abstract of retrieved papers and of the index terms used to describe the articles, and perform a second search in Medline, Embase and Cochrane using all identified keywords and index terms. Third, we will search the reference list of papers included for full text reading for additional sources. We will include experimental and epidemiological study designs, including randomized controlled trials, non-randomized controlled trials, quasi-experimental studies, before and after studies, prospective and retrospective cohort studies, case-control studies, and analytical cross-sectional studies in the scoping review. Qualitative studies, case report, reviews, and conference abstracts will be excluded.

Study selection

We will export the search results to Endnote and remove duplicate studies, then export the results to Rayyan QCRI(13) for screening of titles, keywords and abstract. We will complete the screening and selection of studies in a two-step approach. First, two independent reviewers will screen titles and abstracts to identify potential eligible studies. In case of disagreement, the two reviewers will discuss the disagreement to reach consensus, if they fail to reach consensus, a third reviewer will make the decision. Second, the two pairs of independent reviewers will screen the full text of the potentially eligible studies for inclusion in the scoping review. They will contact the study authors if additional information is required to determine if a study meets the inclusion criteria. Resolving disagreement will follow the same procedure for resolving as for the screening of titles and abstracts. We will document the study selection and outline the process using a PRISMA flow chart. Supplementary File 2 provides a description of selection sources and results extraction. Before starting the screening and selection of studies, the two reviewers will pilot the source selection using a random sample of 25 title and abstracts, discuss any disagreements and make necessary modifications to the eligibility criteria. The screening will start when agreement between the reviewers is 75% or higher.

Charting the data

We will extract the data and provide a logical and descriptive summary of the results for effects of aerobic exercise in the eye (physiological adaptation and impact on pathophysiology), main concepts of measurements (eye related outcome measures) and sources of measurements (methods of examination). In the three summary tables, we will include key information of the source (Author(s),

148 title, year of publication, country, study design, aim, population, sample size, type of aerobic
149 exercise) and results or findings relevant to the review questions (physiology, pathophysiology,
150 outcome measures and examination methods), Supplementary File 2. A trial of the extraction form
151 by two independent reviewers on three sources provides a pilot for data extraction to ensure
152 extraction of all relevant results. Further, if indicated during the review process, we will refine the
153 data extraction and update the charting tables, allowing the charting of results to be an iterative
154 process.

155 Collating, summarising and reporting the results

156 First, we will collate and summarize the results from the data extraction to provide a narrative map
157 of measurement methods of the effect of aerobic exercise in the eye, and potential knowledge gaps.
158 (14) A descriptive, deductive content analysis(15) will disclose physiological adaptations to aerobic
159 exercise in the eye, impact of aerobic exercise on pathophysiology in eye, the eye structures used as
160 outcome measures for effect of aerobic exercise, and methods of examination used to assess the
161 effect of aerobic exercise in the eye. Second, we will provide a critical appraisal of the included
162 studies and report the risk of bias of using RoB 2 (A revised tool to assess risk of bias in randomized
163 trials), ROBINS-I (Risk Of Bias In Non-randomized Studies - of Interventions) and AXIS (Appraisal tool
164 for Cross-Sectional Studies).(16–18) Reporting will follow PRISMA guidelines(19) and text, tables and
165 bubble diagrams will present the results of the scoping review.(14)

167 Patient and Public Involvement statement

168 Information scientists or potential stakeholders is not involved in the conception, design or planning
169 of the study. Consulting expert opinions from researchers at the National Centre of Optics, Vision and
170 Eye Care and the research Health & Exercise – A Life Course Perspective before dissemination
171 ensures broad discussion of the findings.

173 Discussion

174 Visual impairment has a negative impact on wellbeing and quality of life, and the World Health
175 Organization has set a global agenda to reduce the burden of eye disease and vision loss. Aerobic
176 exercise is shown to improve blood flow in eye and prevent the pathogenesis of retinal disease.
177 Moreover, recent advances in technology has transformed retinal imaging and our understanding of
178 the pathogenesis of retinal disease. Existing imaging techniques can provide reliable vascular maps
179 and visualize vascular changes, as well as adaptations to aerobic exercise. However, to date no
180 review has provided a thorough knowledge overview of existing methods used to measure
181 adaptations to aerobic exercise in the eye. This paper describes the protocol of a scoping review with
182 aim to provide a map of methods of measurement of the effect of aerobic exercise in the human eye
183 and potential knowledge gaps related to methods and application of the eye as an outcome measure
184 of aerobic exercise in research and clinical practice. The protocol outlines the methods of the
185 proposed scoping review and ensures research integrity and transparency, as well as replicability for
186 future research. The scoping review can generate recommendations and implications for primary
187 research and/or other reviews. However, recommendations for practice or policy are outside the
188 scope of this review.

191 [List of abbreviations](#)

192 AO; adaptive optics (AO)
193 AXIS; Appraisal tool for Cross-Sectional Studies
194 FAF; fundus autofluorescence
195 OCTA; optical coherence tomography angiography
196 PAM; photoacoustic microscopy
197 PRISMA-ScR; Preferred Reporting Items for Systematic Reviews and Meta-Analysis extension for
198 Scoping Reviews
199 RoB 2; A revised tool to assess risk of bias in randomized trials)
200 ROBINS-I; Risk Of Bias In Non-randomized Studies - of Interventions
201 rMRO2; retinal metabolic rate of oxygen
202 SLO; scanning laser ophthalmoscopy (SLO)
203 sO2; oxygen saturation of haemoglobin

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205 [Declarations](#)

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218 VS contributed to the conception of the design of the work, drafted the protocol, critically revised
219 the protocol and finally approved the version to be published.
220 HRP contributed to the conception of the design of the work, critically revised the protocol and
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222 EMS contributed to the conception of the design of the work, critically revised the protocol and
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