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Systematic review protocol for retinal OCT image analysis of murine models of Alzheimer's disease: findings, methodology and future perspectives

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ADMINISTRATIVE INFORMATION

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Review Stage at time of this submission - The review is completed but unpublished and for this reason the authors register the protocol retrospectively. The protocol was not registered prospectively because the authors were required to do so by the editorial board of the journal to which it was submitted for peer review after the manuscript was finalised. In addition, the editorial board has not started processing the article as it considers it essential to have the systematic review protocol registered.

Conflicts of interest - There are no economic or financial conflicts of interest. Previous work by the authors of this article has been included in the review, however, this has not conditioned the way in which the review has been carried out.

INPLASY registration number: INPLASY202410073

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 17 January 2024 and was last updated on 17 January 2024.

INTRODUCTION

Review question / Objective The aim of this systematic review is to review the different methods of OCT analysis that have been performed in murine models of AD and to analyse which type of OCT has been used, which retinal sectors have been analysed, as well as the segmentation of the retinal layer and which software has been used for this purpose. In addition, we aim to provide a series of recommendations to overcome the challenges encountered in the use of OCT in murine models of AD.

To this end, the proposed systematic review will address the following question: What is the most appropriate methodology for analysing retinal images with OCT in murine models of AD?

Rationale This systematic review is justified by the lack of agreement on protocols for OCT retinal analysis in murine models of Alzheimer's disease.

Condition being studied Alzheimer's disease (AD) is considered the leading cause of dementia (up to 70% of all cases) and it is believed that up to 152 million people will be affected by 2050 (1).The pathophysiology of the disease is characterised by abnormal processing and clearance of two proteins: amyloid-beta (Aβ) and phosphorylated tau (p-Tau), which are believed to lead to a neurotoxic inflammatory process, neuronal dysfunction and ultimately neuro-degeneration (2–4). The disease begins up to 20 years before cognitive signs appear and this period is critical in the search for early diagnosis and future treatment (5).

In patients with AD, structurally changes in the thickness of different retinal layers in the macular area and in the thickness of the retinal nerve fibre layer (RNFL) in the peripapillary area have also been reported (6–9). For this reason, retinal analysis by optical coherence tomography (OCT) has been proposed as a good biomarker for early detection and monitoring of AD-related changes in the central nervous system (10).

To better understand the pathogenesis of AD in the retina, transgenic murine animal models have been used to analyse the deposits of Aβ plaques and neurofibrillary tangles or the neurodegeneration that occur in the retina (11). Histological evaluation has contributed to understanding the mechanisms and pathophysiology of the disease (12), but with the advance of technology, OCT has become one of the techniques currently used because allow in vivo analysis of the retina and thus being able to analyse the model at different time-points, allowing longitudinal studies to control the disease progression and follow-up the secondary therapeutic effects (13).

There are few OCTs adapted to the eye of murine models, and in many cases, devices manufactured or modified by the researchers themselves are used (14). As with clinical OCT, data collection protocols are not homogeneous and there is no consensus as to which areas are the most important for this analysis.

METHODS

Search strategy We performed a literature search up to April 2023 using “MESH” terms in PubMed and Scopus. This review was performed in accordance with the PRISMA 2020 Statement guide-lines. The terms used were: “Alzheimer’s mouse model”, “Optical Coherence Tomography”, “retina ….as well as their combinations.

The search resulted in indexed articles (67 and 109 references from PubMed and Scopus, respectively). After removing duplicates (n=62), a total of 114 articles were ana-lysed. After screening of titles and abstracts, 50 studies were excluded and only 64 full-text studies were retrieved and assessed for final eligibility. In addition, 50 articles were excluded for the following reasons: articles using OCT in mouse models of other diseases (n =33); investigations not using OCT (n =15); investigations in human AD patients (n =2). Finally, 14 studies were included in the systematic review.

Participant or population The studies used in the systematic review include only populations of murine models of Alzheimer's disease.

Intervention In all the articles included in the systematic review, optical coherence tomography of a murine model of AD has been performed. Variations that have been considered for this review include: The murine model of AD, as well as control animal, ages and sex.The eye analysed in each study.The OCT model used.The image acquisition protocol and the retinal sectors analysed.The segmentation of the different layers and the software used for it.The different findings found in each study.

Comparator Not applicable.

Study designs to be included Both cross-sectional and longitudinal case-control studies have been included.

Eligibility criteria We filter the articles by author criteria: the terms had to be in the title, in the abstract or in the article and they should be written in English or Spanish. These papers should clearly explain the OCT analysis techniques that were carried out on an animal model of AD. In addition, we consider articles that will help us better understand the anatomy of the mouse retina, as well as the use of murine retinas in disease research.

Information sources The authors have used bibliographic databases: Pubmed, belonging to MEDLINE and Scopus belonging to Elservier.

Main outcome(s) The number of studies conducted thus far is limited, and there is a lack of consensus regarding examination criteria and the specific areas analysed. Therefore, it is crucial to establish a standardized protocol for the analysis and representation of results in order to facilitate comparability and enhance the validity of findings.

Data management Study and analysis of the papers obtained in the selective bibligraphic review.

Quality assessment / Risk of bias analysis The results and conclusions obtained from this systematic review are not applicable to the practice of evidence-based medicine, as it deals with the analysis of murine models of Alzheimer's disease. The conclusions of this work cannot support that any of the protocols reviewed in the included works are adequate and therefore more work and unification of criteria in the study of the retina with OCT of these animal models is needed.

Strategy of data synthesis In this systematic review, a qualitative approach has been used for the study of the different variables described above (see intervention point). In addition, these data have been summarised in tables to facilitate the reading and understanding of the manuscript.

Subgroup analysis Not applicable.

Sensitivity analysis Not applicable.

Language restriction The analyzed estudies should be written in English or Spanish.

Country(ies) involved Spain.

Keywords Alzheimer's disease; AD mouse model; Optical coherence tomography; retina.

Dissemination plans The authors will present the results in national and international congresses specialised in vision sciences, as well as disseminate the publication in the social networks of the Ramón Castroviejo Ophthalmology Research Institute. Among other transfer and dissemination activities, the authors will communicate the publication of the manuscript to the scientific culture unit of the UCM who will usually publish a press release and send it to the media.

Contributions of each author

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References

1. World Health Organisation. Dementia. 2021 [cited 2021 Aug 11]. Dementia. Available from: https://www.who.int/news-room/fact-sheets/detail/dementia
2. Selkoe DJ. Normal and Abnormal Biology of the beta-Amyloid Precursor Protein. http://dx.doi.org/101146/annurev.ne17030194002421. 2003 Nov 28;17:489–517.
3. Walker LC. Aβ Plaques. Free Neuropathol. 2020;1.
4. Pimplikar SW. Reassessing the amyloid cascade hypothesis of Alzheimer's disease. International Journal of Biochemistry and Cell Biology. 2009;41(6):1261–8.
5. Dubois B, Hampel H, Feldman HH, Scheltens P, Aisen P, Andrieu S, et al. Preclinical Alzheimer's

disease: Definition, natural history, and diagnostic criteria. Alzheimer's and Dementia. 2016;12(3):292–323.
6. Salobrar-García E, de Hoz R, Ramírez AI, López-Cuenca I, Rojas P, Vazirani R, et al. Changes in visual function and retinal structure in the progression of Alzheimer's disease. PLoS One. 2019;14(8):e0220535.
7. Garcia-Martin ES, Rojas B, Ramirez AI, de Hoz R, Salazar JJ, Yubero R, et al. Macular thickness as a potential biomarker of mild Alzheimer's disease. Ophthalmology. 2014;121(5):1149–1151.e3.
8. Lad EM, Mukherjee D, Stinnett SS, Cousins SW, Potter GG, Burke JR, et al. Evaluation of inner retinal layers as biomarkers in mild cognitive impairment to moderate Alzheimer's disease. PLoS One. 2018;13(2):e0192646–e0192646.
9. Trebbastoni A, D'Antonio F, Bruscolini A, Marcelli M, Cecere M, Campanelli A, et al. Retinal nerve fibre layer thickness changes in Alzheimer's disease: Results from a 12-month prospective case series. Neurosci Lett. 2016 Aug 26;629:165–70.
10. Majeed A, Marwick B, Yu H, Fadavi H, Tavakoli M. Ophthalmic Biomarkers for Alzheimer's Disease: A Review. Front Aging Neurosci. 2021 Sep 10;13:574.
11. Jankowsky JL, Zheng H. Practical considerations for choosing a mouse model of Alzheimer's disease. Mol Neurodegener. 2017 Dec 22;12(1):1–22.
12. Ferguson LR, Grover S, Dominguez JM, Balaiya S, Chalam K V. Retinal Thickness Measurement Obtained with Spectral Domain Optical Coherence Tomography Assisted Optical Biopsy Accurately Correlates with Ex Vivo Histology. PLoS One. 2014 Oct 31;9(10).
13. Fischer MD, Huber G, Beck SC, Tanimoto N, Muehlfriedel R, Fahl E, et al. Noninvasive, in vivo assessment of mouse retinal structure using optical coherence tomography. PLoS One. 2009;4(10).
14. Ochakovski GA, Fischer MD. Phenotyping of Mouse Models with OCT. In: Methods in Molecular Biology. 2019. p. 285–91.