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Study of retinal structure and function in retinal disease

Submission date
05/09/2023

Recruitment status
No longer recruiting

Registration date
09/11/2023

Overall study status
Completed

Last Edited
24/06/2024

Condition category
Eye Diseases

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
The leading cause of blindness among working age adults in the UK are inherited diseases that affect the light sensitive cells (the photoreceptors) at the back of the eye (the retina). Imaging the retina and measuring the function are important in these cases to diagnose and monitor disease. Sensitive measures of the retina's structure and function are also highly important in measuring changes in response to new treatments that are being trialled. Standard imaging techniques are limited by the optical properties of the front of the eye which causes optical aberrations (changes to how light rays are reflected that causes blurring of images). Adaptive optics (AO) can be applied to standard imaging techniques used in ophthalmology such as the scanning laser ophthalmoscope (SLO) to correct for these changes to achieve detailed images that allow individual cells to be seen, particularly the photoreceptors. However, AO is a relatively new technology and therefore it is unclear how to use the information that is possible to get from these images. This study will measure the structure of the retina using AOSLO imaging and compare this to established clinical imaging assessments (optical coherence tomography) and visual level (visual acuity). The study will also look to see how the retinal structure is related to how the retina responds to light with the multifocal electroretinogram (mfERG). The mfERG gives a measure of how well the retina works in small areas of the back of the eye, and can be sensitive to changes in disease. This study will compare how this relationship varies in healthy controls and in a group of those with retinal disease.

Who can participate?
We are recruiting healthy controls to compare to those with retinal disease. This is open to any adult aged 18 -80 years old, with no history of eye problems, who meets driving standard vision (can read car number plate from 20 metres), without significant glasses prescription (up to 4 dioptres or 2 dioptres astigmatism). We are also recruiting participants with late-onset retinal degeneration (L-ORD), who can participate if they have a molecularly confirmed case of L-ORD, are aged between 18-80 years old and have sufficient remaining retinal structure to image. This will be determined by a member of study team or Ophthalmologist.

What does the study involve?
If you were to take part we would ask that we could spend about 60 minutes doing some tests and getting some pictures taken of the back of the eye. We will first ask you some quick

questions about your eyes and past medical history to make sure you are suitable to take part in this study.
The first tests will involve looking at a letter chart and telling a member of the study team how many letters you can read, this gives us a measure of how well you see. The next tests will all involve having eye drops in your eyes that make your pupil large and stops it shrinking in response to light. This lasts approximately 4 hours and means you cannot drive for a period of atleast 4 hours after having them as it can blur you vision slightly. We can provide some reimbursement for travel costs due to this. After your pupils are dilated we will use a camera called an optical coherence tomography (OCT) to image the back of the eye, OCTs are used in normal eye clinics.

We will then perform a multifocal electroretinogram (mfERG). This will involve looking at a screen with black and white hexagons flashing on and off while we record the activity from your eye. To do this we will use sticky-pad electrodes around the eye, on your forehead and small gold foil electrodes will contact the front of your eye, the cornea. This test takes between 5 and 10 minutes once you are set-up. We will also perform a full-field electroretinogram (ffERG), which uses the same electrodes as the mfERG but we will use flashing lights to record how the eye responds. We will do this test in the light and after you have sat in the dark for 20 minutes. This test will take 30 minutes once you are set up. After these tests we will either finish your visit and ask you to come back to Newcastle University on a different day for some more tests or after a short break do the rest of the tests on the same day.

For the second set of tests we will take pictures of the back of your eye with the adaptive optics camera. This will involve looking at targets in the distance while a light is shone into the back of your eye. This can take quite some time, we usually allocate 2 hours to this session so we can give you plenty of breaks.

What are the possible benefits and risks of participating?
As with all medical procedures, there are some small risks. There is a small risk that the pattern on the screen can make some feel slightly sick; this is extremely rare. There is also a small risk that the electrodes that sit under the lower lid could cause a corneal abrasion; however, this can be avoided by avoiding scrunching or rubbing the eyes while these are in place. The eye-drops we use may cause slight discomfort, such as stinging, when they are first administered but this should last only a few seconds.
We will minimise all of these risks by talking you through every procedure and the study team have multiple years of experience in performing the study procedures.
There is currently no direct benefit for the research participants. However, as L-ORD is an inherited disorder the findings of the study could be beneficial to their family members in the future.

Where is the study run from?
Newcastle upon Tyne Hospitals NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
January 2023 to December 2025

Who is funding the study?
National Institute for Health and Care Research (NIHR) (UK).

Who is the main contact?
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Contact information

Type(s)
Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
314281

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
10173, IRAS 314281

Study information

Scientific Title
Studying retinal structure with adaptive optics and function with multifocal electroretinogram

Acronym
REDEFINE

Study objectives
To determine the feasibility of collecting novel images of the retina with an adaptive optics scanning laser ophthalmoscope (AOSLO) in healthy controls and in those with retinal disease to assess how the retinal cells (photoreceptors) are arranged. This will help determine the utility of these measures as a clinical marker of disease in the future.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 06/06/2023, North of Scotland Research Ethics Committee (1) (Summerfield House, 2 Eday Road, Aberdeen, Ab156RE, United Kingdom; +44 1224 558458; gram.nosres@nhs.scot), ref: 23/NS/0049

Study design
Feasibility study

Primary study design
Other

Study type(s)
Other

Health condition(s) or problem(s) studied
Inherited retinal disease, late-onset retinal degeneration

Interventions
Retinal imaging with adaptive optics scanning laser ophthalmoscope and visual electrophysiology with multifocal and full-field electroretinogram.

The healthy controls will be recruited through their voluntary response to a study advert. The late-onset retinal degeneration patients will be recruited from the retinal genetics clinic in the Newcastle Eye Centre. Once recruited the participants will be contacted to organise their visit for the study procedures. All procedures carried out within the Medical Physics department in Newcastle upon Tyne Hospitals NHS Foundation Trust (NuTH) will be undertaken in a single visit. The procedures carried out within the Henry Wellcome building in Newcastle University (NU) will be performed during a separate visit, unless a patient has a preference to undertake this on the same day. We aim to collect one set of data on either one or two visits, dependent on the participants preference. The total time required of the participants is detailed below and will

take approximately 3 hours. If two visits are needed we will be a maximum of 6 months between two visits.

Intervention Type
Other

Primary outcome(s)
1. Recruitment rate recorded as number of eligible participants who consent to participate in study by recruitment end date.
2. Attrition rate, recorded as the number of participants who consent to participate that remain in the study until the end of their involvement in study (after undergoing all study procedures).
3. Success rate of AOSLO imaging sessions in recruited participants in both:
3.1. Healthy controls
3.2. Late-onset retinal degeneration

Key secondary outcome(s))
1. Photoreceptor mosaic metrics measured using Adaptive Optics Scanning Laser Ophthalmoscope (AOSLO) at baseline:
1.1. Photoreceptor density
1.2. Photoreceptor arrangement
1.2.1. Intercell distance
1.2.2. Voronoi analysis
2. Fixation stability measured using AOSLO at baseline.
3. Macular function measured from the amplitude of the P1 component of the multifocal electroretinogram at baseline.
4. Retinal function measured from the amplitude of a- and b-wave components of the full-field electroretinogram at baseline.
5. Retinal thickness measured from optical coherence tomography (OCT) at baseline.
6. Ellipsoid zone intensity measured from OCT at baseline.
7. Visual function measured using:
7.1. The ETDRS visual acuity at baseline (best corrected visual acuity (BCVA))
7.2. The low luminance visual acuity at baselines (ETDRS BCVA +2 neutral density filter)
7.3. Contrast sensitivity measured using Pelli Robson score at baseline.

Completion date
31/12/2025

Eligibility

Key inclusion criteria
1. Control
1.1. Adult between ages of 18 – 80 years old
1.2. Capable of performing all of the tests in the study procedures
1.3. Able to give informed consent to all of the procedures.
2. Late-onset retinal degeneration
2.1. Adult between ages of 18 – 80 years old
2.2. Capable of performing all of the tests in the study procedures
2.3. Able to give informed consent to all of the procedures
2.4. Have a confirmed genetic diagnosis of L-ORD

Participant type(s)

Healthy volunteer, Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
80 years

Sex
All

Key exclusion criteria
1. Healthy control
1.1. Younger than 18 and older than 80 years old
1.2. Inability of participant to provide informed consent
1.3. Withdrawal of consent
1.4. BCVA of less than 6/12 in either eye
1.5. Participants with a spherical equivalent of greater than 4 dioptres or astigmatism greater than 2 dioptres
1.6. Taking any medication that can affect retinal function (e.g. Hydroxychloroquine, Deferasirox, Vigabatrin).
1.7. Known to have any ocular condition that will affect test results/ability to test:
1.7.1. Inherited retinal condition
1.7.2. Glaucoma
1.7.3. Age related macular degeneration
1.7.4. Amblyopia
1.7.5. Nystagmus
1.7.6. Corneal or other media opacity
1.8. Known to have any medical condition that will affect test results/ability to test:
1.8.1. Epilepsy
1.8.2. Raised intracranial pressure
1.8.3. Multiple sclerosis.
2. Late-onset retinal degeneration
2.1. Younger than 18 and older than 80 years old
2.2. Inability of participant to provide informed consent
2.3. Withdrawal of consent
2.4. Participants with a spherical equivalent of greater than 4 dioptres or astigmatism greater than 2 dioptres
2.5. Have loss of sufficient retinal structure to image (absent or substantially disrupted ellipsoid zone on SD-OCT)
2.6. Taking any medication that can affect retinal function (e.g. Hydroxychloroquine, Deferasirox, Vigabatrin)
2.7. Known to have any ocular condition that will affect test results/ability to test:
2.7.1. Nystagmus
2.7.2. Corneal or other media opacity

2.8. Known to have any medical condition that will affect test results/ability to test:
2.8.1. Epilepsy
2.8.2. Raised intracranial pressure
2.8.3. Multiple sclerosis.

Date of first enrolment
10/09/2023

Date of final enrolment
30/11/2025

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
The Royal Victoria Infirmary and Associated Hospitals NHS Trust
Queen Victoria Road
Newcastle upon Tyne
United Kingdom
NE1 4LP

Study participating centre
University of Newcastle Upon Tyne
Claremont Road
Newcastle upon Tyne
United Kingdom
NE1 7RU

Sponsor information

Organisation
Newcastle upon Tyne Hospitals NHS Foundation Trust

ROR
https://ror.org/05p40t847

Funder(s)

Funder type
Government

Funder Name
NIHR Academy

Funder Name
NIHR Research capability funding (NUTH)

Results and Publications

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 1.0	30/05/2023	08/09/2023	No	Yes
Participant information sheet	Control group version 1.0	30/05/2023	08/09/2023	No	Yes