**Neural mechanisms of visual plasticity in amblyopia**

# PARTICIPANT INFORMATION SHEET

Version 1.0, 03.03.2023

Central University Research Ethics Committee Approval Reference: R80950/RE001

We would like to invite you to take part in a research project. This sheet provides some information to help you decide whether to do so. Please take time to read this carefully and discuss it with friends, family or your GP if you wish. If there is anything that you do not understand, or if you would like more information, please ask us. Please take time to consider whether you wish to take part.

What is the purpose of the research?

We are interested in understanding how the brain is organised, processes information and performs skills such as seeing with both eyes. We can investigate this by using a safe technique called Magnetic Resonance Imaging (MRI) to scan the brain.

Some people have a ‘lazy eye’ which means that the input to the brain from the left and right eye was not equal when they were children. Lazy eye, also known as amblyopia, is thought to be linked to the function of the visual part of the brain, and the signals that control information processing in the brain. Visual training improves vision in some people with lazy eye. The question we hope to answer is what happens in the brain when people with lazy eye use visual training. By answering this question, we hope to better understand the relationship between visual changes and brain signals.

Why have I been invited to take part?

You have been invited to take part in this research because you may have lazy eye or have been diagnosed with lazy eye by an orthoptist. We will be recruiting up to 45 participants in this study. Please get in touch if you are not sure whether you meet inclusion or exclusion criteria.

To be eligible, you:

* Have been recently been diagnosed as having a lazy eye by an orthoptist (< 3 years), or suspect you have lazy eye and are willing to attend a screening (organized by us) to confirm this.
* Have an up-to-date visual prescription (< 2 years).
* Are English speaking, and willing and able to give informed consent for participation in the study.
* Are a healthy adult, aged 18 to 50 years.
* Are not currently taking any medications (except the contraceptive pill).
* Are not pregnant or breast feeding.
* Have no orthoptic or ocular abnormality other than lazy eye or visual correction.
* Have no neurological or psychiatric abnormality.
* Have no MR Spectroscopy specific contraindications e.g. use of antipsychotic medication, history of migraine, frequent cigarette and/or alcohol consumption.
* Have sufficient vision in your lazy eye to take part in the visual training. This is established based on your notes from the orthoptist.
* Have a reliable internet connection at home (mandatory for the duration of the visual training regime).

If you have MRI contraindications e.g. presence of metallic implants, a pacemaker, recent surgery etc. you will be able to participate as a control. Please see the details about what this would involve on page 4.

Do I have to take part?

No. It is up to you to decide if you want to take part in this research. We will describe the research, go through this information sheet with you, and answer any questions you may have. If you agree to take part, we will ask you to sign a consent form and will give you a copy for you to keep. However, you would still be free to withdraw at any time, without needing to give a reason. This would not affect legal rights you would receive. If you are a student at the University of Oxford or Oxford Brookes, there would be absolutely no academic penalty if you decide you do not want to take part, or if you decide to withdraw at any point.

What will happen to me if I take part in the research?

Once you express your interest over email or telephone, a researcher will contact you to go over the participant information sheet, this is the sheet you are reading right now, explain what is involved for participants and go through a screening form with you to check if it is safe for you to participate. To ensure that you are safe to participate, we will ask you questions about your medical history. If you have a history of eye patching or unbalanced binocular vision, you will also be asked to describe your history of binocular vision, including any treatments and medical procedures relating to your vision. To check if your vision may be unequal between eyes, we may ask you to test your visual acuity at home, using a phone app and an online app hosted on Pavlovia.org, or ask for your most recent optician’s report which you would supply to us. Please note that you will need an up-to-date (<2 years) visual prescription to ensure that your eyesight is corrected prior to commencing the visual training study.

Then, for prospective participants, we will ask you to fill out a digital screening consent form for an orthoptic screening; we will send a link via email for you to complete this online. If you consent you will be invited to take part in a 30 min orthoptic screening visit at the Oxford Eye Hospital, John Radcliffe Hospital, Headington, Oxford, where a trained eye specialist will formally assess your binocular vision and give you an opportunity to ask any questions you may have about your binocular vision.

The aim is to establish a clinical diagnosis of amblyopia. This session will be offered only to participants who report unbalanced vision due to having a lazy eye, and who have no recent records (past 3 years) of orthoptic assessment. This session will be free of charge and can be booked at your convenience. We will offer you a formal invitation to the study if you are diagnosed with amblyopia.

If you agree to take part, you would attend an inclusion visit at the FMRIB Building (WIN Centre) at the John Radcliffe Hospital Site in Headington, Oxford, a pre-training visit a week later , and a post-training visit 3 weeks later. In addition, you would agree to perform a visual training regime on a virtual reality device at your own home between the first and second visit. You would also agree to connect the virtual reality device to your internet network every time you perform the experiment at home. The visual training consists of 15 x 1 h training on a visual task. The 15 x 1h sessions can be spread out over the period of 3 weeks.

On the first visit, i.e. inclusion visit, we would ask you to **bring your most recent visual prescription to the visits** (which needs to be within the past 2 years).

 The pre-training visit, as well as the post-training visit may include a non-invasive brain scan lasting up to 120 min, and visual tests lasting up to 90 min. Both these tests will be collected within a single research visit, with up to an hour scheduled for breaks. The total duration of each visit is approximately 5 hours (2 h MRI scan, 1.5 h visual tests and 0.5 h break 0.5 h preparation). Please leave enough time for your visits. Please let us know beforehand if you wear contact lenses or glasses.

1. **Visit 1:** The 30-minuteorthoptic screening visit at the Oxford Eye Hospital, John Radcliffe Hospital, Headington, Oxford, where a trained eye specialist will formally assess your binocular vision and give you an opportunity to ask any questions you may have about your binocular vision. No eye drops will be used during this visit.
2. **Visit 2:** Following the orthoptist visit, if you are happy to continue, the researchers will then ask you to sign and date two copies of a consent form. One copy is to keep for the researcher, one for you to take home. You will then undertake a visual test session. The visual test session consists of a series of computerised visual tests taking place at the same WIN-FMRIB centre and will take approximately 120 minutes. You will take part in a series of computerised visual acuity tests and binocular vision tests that assess your ability to combine information using your two eyes on simple repetitive tasks (i.e. ‘judge the position in depth of a circle’). You will be encouraged to rest between each run if your eyes get tired.
3. **Visit 3:** On arrival at WIN-FMRIB, one of our research team will meet you to describe what participation will involve and answer any questions you may have. The researcher will go through an MRI safety Screening Form again to make sure that it is safe for you to participate in the research. If you are happy to continue, they will then ask you to sign and date two copies of a consent form. One copy is to keep for the researcher, one for you to take home. If you have a squint, the researcher will select MRI-safe prism glasses to allow your eyes to fixate on the same point in space. The paragraphs below describe what is involved in the brain scan and visual test session.
	1. **Brain scan**: You will undergo MRI-safety screening with the radiographer or scan operator and then change into MRI-safe pyjamas. Once declared safe, you can enter the 3T-console room and undergo MRI scanning. During the scan, you will be instructed to lie as still as possible on a table. We will try to measure the position of your eyes during the scan by using a non-invasive, contact-less infrared eye tracker. The eye tracker uses the reflections off your pupil to record the co-ordinates of where your eyes are looking – no images will be taken. For this, a short calibration procedure will be performed at the beginning of your scanning session, where you will look at different dots appearing on the screen. The research would involve having a series of magnetic resonance scans over a period of 120 minutes.
	2. **Visual tests**: The visual test session consists of a series of computerised visual tests taking place at the same WIN-FMRIB centre and will take approximately 90 minutes. You will take part in a series of computerised visual acuity tests and binocular vision tests that assess your ability to combine information using your two eyes on simple repetitive tasks. This session is similar to what you performed during the inclusion visit. You will also perform a subset of the tests on a virtual reality device. You will be encouraged to rest between each run if your eyes get tired.

If MRI scans are missing or poor quality, you may be invited to return to the laboratory, provided you have not yet commenced your training regimen. During the supplementary MRI scan session, you may repeat either the entire scanning session or specific subsets thereof, depending on the extent of the missing/poor quality measures.

1. **Between Visit 3 & 4 - Virtual Reality Training at Home:**
	1. If you are part of the training group, you will be given a virtual reality device to take home for training between the pre- and post-training visits. The device will be given to you and the researcher will not perform any home visits. You will be provided with a document detailing how to use the Visual Reality Training device and any support you may need in using the device or completing the training can be delivered via email, phone calls or/and virtual conference calls. Before starting the training, you must ensure the virtual reality device is connected to your home internet network. A section in the Virtual Reality Training device instruction sheet is detailing this procedure.
		1. You will be asked to train 15 days at 1h/day, at roughly the same time of day, spread over a period of 3 weeks. Your training will consist of 1h daily performance of a challenging visual task, displayed on the virtual reality headset.
		2. The task is to report which out of two contrast stimuli presented to your weaker eye is stronger (the stronger stimulus is the ‘target’ stimulus), while your stronger eye is shown a ‘noisy’ image. The stronger the noisy image, the more difficult the task. The aim of the task is to detect the target stimulus under increasing strength of the noisy image.
		3. You are encouraged to find a quiet room and to be seated in a comfortable and stable position for the duration of the training. To minimise disruption, you could turn off your phone and computer while you train. You can wear your normal visual prescription underneath the virtual reality device. You are encouraged to take brief breaks to reduce the occurrence of eye fatigue from using virtual reality devices. You imperatively must connect the device to your home Wi-Fi network. If the device is not connected, the session cannot be performed.
		4. Data from your performance is recorded by the virtual reality device and stored in secured Amazon servers. Your data is anonymised and uploaded automatically, only the authorised personnel can access it. . The device will be returned to the researchers after you are finished with visual training at your post-training visit. We kindly ask you not to use the device for any other purpose than the visual training regime and to store it in a safe location.
		5. We may get in touch via email or phone if the online data suggests that you need some support with the training.
2. **Visit 4:**
	1. The post-training visit will follow the same structure as the pre-training visit. You will undergo an MRI scan of 120 min, followed by a break and a 90 min visual test session. The whole visit can last up to 5 hours including breaks. After this visit, you will have completed the study.
	2. You will need to return your Oculus device during this visit.

In the event of missing or poor quality MRI scan data, you may be asked to return to the laboratory for a supplementary MRI scan session. The extent of rescanning, whether encompassing the entire session or specific subsets thereof, will be determined based on the nature of the missing/poor quality measures.

**Control Participants:**

If you have amblyopia (or lazy eye) but are not able to have an MRI scan, there is also the option to take part in the study as a control participant. Control participants will complete Visits 1 and 2 exactly the same as the test participants, but during Visits 3 and 4 they will only complete the visual and behavioural tasks and will not partake in the MRI scan section of the visits. Control participants will also not complete the 3-week Virtual Reality visual training.

***What possible implications of the Orthoptic assessment are there?***

You will have the opportunity to ask the Orthoptist any ophthalmic questions you may have about your eyes. If the Orthoptist detects an incidental finding during the screening tests this will be explained to you, along with management advice the Orthoptist feels is appropriate. If they think you would benefit from a full Orthoptic appointment, this will be discussed with you. You will need to be referred formally via your GP. If the Orthoptist suspects an Opticians visit would be beneficial, this will be recommended. In the event of detecting an ocular abnormality during screening that the Orthoptist feels is an emergency, the Orthoptist will liaise with the Doctors in Eye Casualty. If you do get referred to the Orthoptist or are seen in Eye Casualty then a copy of the screening report will be filed in your NHS notes.

Are there any disadvantages or risks in taking part?

MRI is safe and does not involve any ionising radiation (x-rays). However, because it uses a large magnet to work, MRI scans are not suitable for everybody. You would be asked to answer some safety questions to determine if you can take part. Normally, we would need more information before you take part in the research MRI scan if you have a heart pacemaker or stent, mechanical heart valve, mechanical implants such as an aneurysm clip, joint replacement (e.g. hip/knee), or if you carry other pieces of metal that have accidentally entered your body.

While there is no evidence that MRI is harmful to unborn babies, as a precaution, the Department of Health advises against scanning pregnant women unless there is a clinical benefit.  We do not test for pregnancy as routine so if you think you may be pregnant you should not take part in this research.

While very rare, tattoos can occasionally warm up in the scanner. Please inform the person operating the scanner immediately if you feel any heating. If you have a new tattoo, you should not take part in a scan until 48 hours after receiving the tattoo.

If you think you might be claustrophobic, please talk to the researcher in advance, or let the person operating the scanner know before you start.

Some of the scans are noisy, so we will give you earplugs to make this quieter for you. It is important that these are fitted correctly, as they are designed to protect your hearing.

In preparation for your scan and for your comfort and safety we may ask you to change into scrubs ("pyjama-style" top and trousers), available in a range of sizes. You may keep your underwear and socks on, but you will need to remove underwired bras. If you have a suitable non-wired bra, you may wear this instead. Do not wear any fabrics that contain metallic threads or are silver impregnated (often marketed as anti-microbial/bacterial or anti-odour/stink). Metal jewellery, including body piercing, must also be removed. If you wish to wear eye makeup to your scan, we will give you makeup removal wipes because you should not wear eye shadow or mascara in the scanner. Please bring your own makeup to reapply. Lockers are provided to secure your personal belongings and clothing.

You will be introduced carefully to the scanner and allowed to leave at any stage. Whilst in the scanner you will have a call button, which you can press if you need to stop the scan or speak with the person operating the scanner.

It is important to note that we do not carry out scans for diagnostic purposes, only for research. Our scans are not routinely looked at by a doctor and are therefore not a substitute for a doctor’s appointment. Occasionally, however, a possible abnormality may be detected. In this case, we would have the scan checked by a doctor. If the doctor felt that the abnormality was medically important, you would be contacted directly and recommended to have a hospital (NHS) diagnostic scan arranged. You would not be informed unless the doctor considers the finding has clear implications for your current or future health. All information about you is kept strictly confidential.

Are there any benefits in taking part?

While there are no immediate benefits for those people participating in the project, it is hoped that this research will lead to a better understanding of plasticity of the visual brain in adulthood*.*

Expenses and payments

You will receive £30 for the inclusion visit and £62.50 for each of the pre- and post-training visits (£155 total). We will provide an additional bonus reimbursement of £80 if all 1h/day for 15 days over 3 weeks of training have been performed (totaling £235 if everything is completed). If you are unable to complete a session for any reason other than our equipment malfunction, you will be paid the equivalent amount for the time spent in the session. Any supplementary pre- or post-training visit will be reimbursed accordingly.

Control participants will receive £30 for the inclusion visit and £30 for each of the pre- and post-training visits, as they will not be completing the MRI scans (£90 total)

Travel costs of up to £100 can be reimbursed across all four visits (averaging £25 per visit) if you provide paper or photographic receipts. Reimbursement and compensations are paid upon completion of the study through the Oxford University finance service to your personal bank account; please note this can take up to 10 weeks to come through. If you withdraw before completing the study, we will reimburse and compensate you for your expenses at that point.

What information will be collected and why is the collection of this information relevant for achieving the research objectives?

Below is the list of data we will collect:

* **Initial study screening documents** (identifiable, paper) – Initial screening documents for MRI safety will be collected over the phone or video conferencing, and entries made on paper form corresponding to the most recent MRI safety procedures for 3T scanning. These paper forms will be shredded once the participant has gone through the initial screening. No backup of these records will be made.
* **Screening app task results** (anonymised, electronic) - This data can only be accessed by approved personnel. The data will be stored on the Pavlovia gitlab server as long as we are collecting data. When the study ends, the data will be collected, accessed and stored via a password and firewall protected server at the FMRIB Centre. The data on the Pavlovia gitlab server will be deleted.
* **Screening Consent** (identifiable, electronic) – Screening consent will be obtained from participants who take part in the orthoptic screening, to check if they are eligible for the study. The screening consent will be emailed to participants as a password protected online survey prior to the orthoptic appointment. The form is first filled out by the participant, and then the researchers. The digital forms are thus emailed to both the participant and the researchers.  If the participant is deemed eligible after the screening, then the consent is saved on the University approved firewall and password protected OneDrive storage as a pdf document. If participant is deemed ineligible after screening, then the screening consent will be deleted once the decision has been taken, together with any of the participant's contact details. Screening consent forms will be kept for at least 3 years after publication or public release of the research.
* **Questionnaire: amblyopia/strabismus and quality of life** (pseudoanonymised, electronic) – electronic data from questionnaires will be kept in a password protected Excel file and shared with researchers using University secure online website (sharepoint.nexus.ox.ac.uk).
* **Full Consent Records** (identifiable, paper) – Full consent will be obtained from participants who are eligible for the study. Participant consent using the paper forms will be obtained from participants inside the dedicated participant room at the WIN FMRIB site. The participant will fill out two paper forms, one for the participant to keep and one for the researcher and signed by the participant and researcher. The researcher’s paper consent form will be kept in a locked and secure storage cabinet in the WIN-FMRIB site within the office space of the principal researcher. The participant’s form will be taken home by the participant. Consent forms will be kept for at least 3 years after publication or public release of the research.
* **On the day Study safety screening documents of the MRI scans** (identifiable, paper) - will be kept by WIN-FMRIB radiographers in a locked and secured location at the WIN-FMRIB site.
* **Contact details** (identifiable, electronic) – Electronic contact details of participants will be kept in a password protected Excel file and shared with researchers using University secure online website (sharepoint.nexus.ox.ac.uk). Contact details will be permanently deleted after the end of the study period, except where permission is given to retain these for future contact.
* **Eye tracker video recordings and behavioural response data** (anonymised, electronic) – eye movement data is composed of numerical coordinates (x and y coordinates) of participants is coded at source with an anonymization code that cannot be directly linked to the volunteer. No images of the participants’ face or eyes will be taken. Electronic behavioural response data will be anonymised. Data is collected, accessed and stored via a password and firewall protected server at the FMRIB Centre. Data will be stored for at least 3 years after final publication or public release.
* **Contact details for future studies** (identifiable, electronic) - electronic contact details of potential future participants will be kept in a password protected Excel file and shared with researchers using University secure online website (sharepoint.nexus.ox.ac.uk). Participants will be reminded that they can opt out of this at any point and contact details will then be deleted.
* **MRI scans** (pseudoanonymised, electronic) - Imaging data is automatically coded at source with an anonymisation code that cannot be directly linked to the volunteer. This anonymization code and key is stored with the imaging data on a secure database at the WIN Centre. Authorised scanning centre personnel and the research team will have access to the MRI imaging data. MRI imaging data is assigned a unique ID as it is collected and stored in a secure database within the scanning system. Due to the nature of these images, they remain potentially identifiable, even after we destroy your personal details. Imaging data will be stored on archive tapes indefinitely, even if you withdraw from this research. Any electronic data (behavioural data files) collected during the study will be labelled with a code number rather than a name or initials. Data collected at the WIN-FMRIB site is accessed via a password and firewall protected server at the FMRIB Centre. Data will be stored for at least 3 years after final publication or public release.
* **Visual training and behavioural task results** (anonymised, electronic) behavioural task data is composed of numerical performance measures of participants and is coded at source with an anonymization code that cannot be directly linked to the volunteer. Electronic behavioural response data will be anonymised. Data from the visual training is downloaded and stored in Amazon Web Services (AWS) DynamoB server. This data can only be accessed by approved personnel. The data will be stored on the server as long as we are collecting data. When the study ends, the data will be collected, accessed and stored via a password and firewall protected server at the FMRIB Centre. The data on the AWS DynamoB server will be deleted.
* **Clinical assessment from orthoptists** (anonymised, electronic) – are recorded on a clinical assessment form in paper and electronically scanned and sent to the researcher’s password protected email address as an anonymous electronic file.
	+ Identifiable physical forms (identifiable, paper) - A hard copy of the clinical report will be kept in a folder in secure and locked file cabinets at the Oxford Eye Hospital in the office of the orthoptist, this is separate to the NHS notes. The reports are filed with the participant’s initials and the date they were seen. The hard copy of the report will be kept for at least 3 years after the final publication or public release.
* **Bank details for remuneration** (identifiable, electronic) – Electronic bank details of participants will be sent via email to a password protected University email address, and kept in a password protected Excel file. Bank details will be permanently deleted after the end of the study period.

Identifiable data will be removed whenever possible, and any data transfer will be done securely. All data processing including transfers will comply with UK data protection law. We may use data from this research in future studies and share this with other researchers (e.g. in online databases). This will only be in a form that does not identify you.

The researcher, research team and collaborators will have access to the research data. Responsible members of the University of Oxford may be given access to data for monitoring and/or audit of the research.

With your consent, we will keep your contact details on a secure database in order to let you know about future studies. We will keep a copy of your consent form with this database, as your consent is our legal basis for re-contacting you under UK data protection law. If you are contacted about a future study, you **do not** have to agree to participate. You can have your details removed from the database at any time by contacting the researchers. If you do not consent for your contact details to be kept, they will be deleted as soon as no longer needed for this study.

Research data may be transferred to, and stored at, a destination outside the UK and the European Economic Area. Details that directly identify you will be removed, and any data transfer will be done securely and with a similar level of data protection as required under UK law.

Will the research be published? Could I be identified from any publications or other research outputs?

The findings from the research will be written up in student research projects, academic publications, conference presentations, a report commissioned by an external organisation, websites, videos. It will not be possible for participants to be identifiable from the outputs.

Data Protection

The University of Oxford is the data controller with respect to your personal data and, as such, will determine how your personal data is used in the research.

The University will process your personal data for the purpose of the research outlined above. Research is a task that we perform in the public interest.

Further information about your rights with respect to your personal data is available from <https://compliance.web.ox.ac.uk/individual-rights>.

Who has reviewed this research?

This study has ethics approval from a subcommittee of the University of Oxford Central University Research Ethics Committee (Ethics reference: **R80950/RE001**).

Who is organising and funding the research?

The research is organized by Dr Betina Ip, a researcher at the University of Oxford. It is funded by a Royal Society Dorothy Hodgkin Fellowship to Dr Ip and a Medical Research Council research grant to Professor Holly Bridge and Dr Ip.

Who do I contact if I have a concern about the research or I wish to complain?

If you have a concern about any aspect of this research, please contact Dr Betina Ip (01865 611456, betina.ip@ndcn.ox.ac.uk) and I will do my best to answer your query. I will acknowledge your concern within 10 working days and give you an indication of how it will be dealt with. If you remain unhappy or wish to make a formal complaint, please contact the Chair of the Medical Sciences Interdivisional Research Ethics Committee (MS IDREC) at the University of Oxford who will seek to resolve the matter as soon as possible - Email: ethics@medsci.ox.ac.uk; Address: Research Services, University of Oxford, Boundary Brook House, Churchill Drive, Headington, Oxford OX3 7GB.

Further Information and Contact Details

If you would like to discuss the research with someone, or if you have any questions, please contact:

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