Note: This Approved Procedure can be combined with Approved Procedure CUREC_AP_IDREC_03 "Studies Involving Electrophysiological Recordings from the Scalp in Adult Volunteers" and/or Approved Procedure CUREC_AP_IDREC_08 "Studies Involving Magnetoencephalographic (MEG) Recordings from Adult Volunteers"

STUDIES USING PSYCHOPHYSIOLOGICAL METHODS WITH ADULTS

1. SCOPE

This Approved Procedure covers specific psychophysiological recording methods in adult volunteers, more precisely physiological recordings specified in the CUREC glossary as "invasive procedures (Class B, i.e. minimally or non-invasive)"
It includes:

- eye movement recording by electrooculogram (EOG)
- electromyography (EMG)
- Near Infrared Spectroscopy (NIRS)
- recording of heart rate by electrocardiogram (ECG)
- skin conductance response (SCR) / galvanic skin response (GSR) – for details see Appendix A
- eyeblink conditioning
- functional transcranial Doppler ultrasonography (fTCD) – for details see Appendix B
- high-resolution retinal imaging with an adaptive optics enabled instrument, such as an adaptive optics scanning laser ophthalmoscope (AO-SLO), or adaptive optics optical coherence tomography (AO-OCT) – for details see Appendix C

This procedure may be combined with Approved Procedure 03 to conduct recording of electroencephalogram (EEG), or with Approved Procedure 08 for magnetoencephalography (MEG). If the procedures listed above are to be combined with either EEG or MEG, requirements specified in this Approved Procedure (AP_IDREC_18) and in the Approved Procedures for EEG or MEG have to be met.

2. TRAINING OF RESEARCH STAFF

Training in application of physiological equipment and setting up the recording must be given by a researcher with appropriate experience in the particular technique being used, and no inexperienced person should be left in sole charge of a physiological study.
Where air cylinders are involved, researchers should have attended a gas cylinder safety course.
Where lasers or other powerful light sources are present in the laboratory, researchers must have attended a laser safety course. Where eye drops are used to dilate the pupil to improve the quality of retinal images, researchers must have attended a training session, and demonstrated competency.

Before beginning research, new researchers will:

- Read and agree to the relevant sections of CUREC Best Practice Guidance 09 'Management and Protection of Data Collected for Research Purposes'
- Complete the University's Research Ethics and Integrity training or equivalent

- Receive satisfactory methodological training from the Principal Investigator or designee, such that the Principal Investigator is satisfied that they may conduct research independently

While training is ongoing, new researchers may 'shadow' experienced researchers, but **will not** a) seek consent from the participant, or b) gain access to identifiable data. During this period, new researchers will be able to familiarise themselves with the procedures of the research group, according to current documentation, including the details of this Approved Procedure. Once satisfactory training has been signed off, the new researcher may conduct research independently and have full access to identifiable data concerning participants.

3. METHODS FOR RECRUITING PARTICIPANTS

Potential participants will be identified using one of the methods outlined in the application. When a potential participant registers interest, further information (prepared with the associated template information sheet) will be given, together with details on how to confirm that they would like to take part.

4. INFORMATION PROVIDED TO PARTICIPANTS

Researchers should be aware that the unfamiliarity of physiological recordings may in itself cause anxiety. The information sheet should, if possible, contain a picture demonstrating what will be involved in the physiological recording, in addition to the usual verbal description. Researchers may also consider making a short video recording showing what is involved; this could be distributed to potential participants or made available on a website to help participants decide whether to take part.

Where relevant, it is recommended that the word 'sensors' be used rather than 'electrodes' when describing a procedure.

The information sheet must make it clear that the procedure is for research and is not designed to identify health problems, and that the researcher has no training in identifying health-related problems from the recordings. A section such as the following may be included in the information sheet: "In the unlikely event of the researchers noting an irregularity in the recording they would discuss this with a clinical specialist and inform you if it was felt necessary for you to discuss further with your GP." (The precise wording might need modifying depending on the specific procedure).

The Information Sheet must be written in simple but non-patronising language. Most word-processing packages provide readability statistics for a document, and one should aim for a 12-year-old (Year 7) reading level for adults.

For studies involving electrodermal responses (skin conductance response (SCR) / galvanic skin response (GSR)) or functional Transcranial Doppler Ultrasonography (fTCD), please use the appropriate template information sheet associated with this Approved Procedure.

For all other studies, please see our template information sheet (under the heading 'templates').

5. CONSENT OF PARTICIPANTS

Written consent will be obtained from all participants using the **Consent Form associated with this Approved Procedure.**

Written consent will be obtained from all participants on the day of the first session, following a suitable (at least 24 hour) period during which they will have had an opportunity to read the Information Sheet and discuss their participation with others and with the researchers. An experienced researcher will answer all questions before consent is obtained. Consent will be taken by a member of the research team who has appropriate training, as confirmed by the Principal Investigator. Participants will be reminded that they can change their mind and withdraw from the study at any point without penalty. Vulnerable populations or participants who are unable to provide informed consent in English are not covered by this Approved Procedure.

Copies of the signed consent forms will be provided to the participants along with the information sheet. The originals will be kept in the files of the researchers.

Please also see CUREC's guidance on the informed consent process.

6. COMPENSATION

Compensation (either financial or in-kind) may be offered to participants for their time and travel expenses. Some studies (for example, those investigating reward processing) may involve a performance-related reward. Individual proposals will detail the value (if any) of compensation. Compensation is limited to the time and inconvenience incurred as well as reasonable travel expenses and will under no circumstances consist of course credits for student participants.

Consideration should be given to how and when participants are told about any recompense. Participant information sheets and recruitment materials should state that recompense will be made so that potential participants are not discouraged from participating by the associated costs. As a general rule, recruitment material should not state the value. However, if this is necessary (e.g. it is a requirement of a third-party recruiter), advertisements must not emphasise the value of the payment (for example, through the use of formatting). Further guidance is available within CUREC's Best Practice Guidance 05 on Payments and incentives in research.

7. POTENTIAL RISKS TO PARTICIPANTS/RESEARCHERS/OTHERS AND WHAT WILL BE DONE TO MINIMISE

All the procedures covered by this Approved ProcedureAO-SLO have been used safely for many years. The AO-SLO is a more specialised technology, but has been used widely in vision research labs, including with patients with eye disease[1][2]. We are not aware of any cases of adverse events associated with these procedures.

Nevertheless, although the equipment itself is safe, a physiological laboratory can contain hazards, and researchers should be alert to potential dangers from trailing wires, uncovered sockets, heavy air cylinders, dim lighting or lasers. These will be covered by relevant Health and Safety procedures, and researchers must familiarise themselves with these and be vigilant in monitoring them.

[1] Roorda A, Williams DR. The arrangement of the three cone classes in the living human eye. Nature 397 (6719); 520-2 (1999).

[2] Roorda A, Romero-Borja F, Donnelly III WJ, Queener H, Hebert TJ, and Campbell MCW, Adaptive optics scanning laser ophthalmoscopy, Opt. Express 10; 405-412 (2002).

In addition, where sounds or other stimuli are presented in the course of a study, it is important to ensure that the level is controlled. The researcher should always test the sound level before any auditory test to ensure that there is no risk of damaging the hearing of the participant; where air puffs are presented as stimuli, the level must be regulated so it cannot go above 7 psi; where light is used to image the eye the level of light at the eyepiece must be checked with a power meter before a participant looks into the instrument. Where the equipment produces noise, headphones will be available to enhance participant comfort.

During the session, the researcher should monitor the participant carefully, and if they show signs of distress or discomfort, they should be asked if they want to stop the procedure. It should be possible to pause the procedure if a participant needs to take a break or visit the bathroom, and the procedure will need to be paused if a fire alarm goes off.

If the procedure requires skin contact, a further consideration for researchers is hygiene: electrodes, headsets and instruments used to apply gel must be cleaned/disinfected after each use; if necessary, participants may wash off gel at the end of the session, and freshly laundered towels should be provided. Anti-allergenic gel and cleaning solutions should be used. Where dental impressions are used for head-stabilisation during retinal imaging, each participant will receive a fresh piece of impression compound on a support structure, prepared by the researcher. The participant will hold the support structure and bite into the soft compound to make their own impressions. At the end of the session, the dental impressions will be destroyed and the support structure cleaned/disinfected. Where eye drops are administered to dilate the pupil for retinal imaging, the trained researcher will adhere to specific guidelines for the drops, including hand washing.

Physiological responses vary from individual to individual. Researchers should not to make any judgemental comments on the type of responses seen in individual participants, to avoid causing unnecessary anxiety, e.g. the researcher should not comment such as “you’ve only got very small responses”.

Risks to researchers: The main way to avoid risk is to adhere to a regime of hygiene. Hands are washed after any contact with the skin or saliva of a participant.

8. MONITORING AND REPORTING OF ADVERSE OR UNFORESEEN EVENTS

If a participant should become unwell during the test session, the session will be terminated. Such a case will be reported in the Departmental Safety Book and discussed with the study’s principal investigator. The appropriate CUREC Subcommittee Secretariat will also be informed where the adverse event was deemed related (resulted from administration of any of the research procedures) and unexpected (the type of event is not listed as an expected occurrence).

9. COMMUNICATION OF RESULTS

It is unlikely that results from experimental physiological recordings will be meaningful to people other than the researchers. It should be made clear to participants from the outset that the procedure does not have diagnostic significance.

10. DATA MANAGEMENT AND PROTECTION

The research must be conducted in accordance with the Research Data Policy; CUREC's Best Practice Guidance 09 on Data collection, protection and management; and Research Data Oxford's guidance on data backup, storage and security.

Participants' informed consent must be obtained for participation in the study, which includes the collection, storage and retention of all data related to the study. Directly identifiable personal information held by the research team (such as contact details, consent forms and screening forms, which include name or other identifiers) must be held securely - either in paper format in lockable filing cabinets with access only by the University researchers, or in a password-protected database, on an encrypted machine or on a protected server. These should be servers provided by the University where the risks and access have been professionally managed. Other servers will require security assessment by University Information Security. Other research data (e.g., EEG files, behavioural reaction time files, questionnaires) must be labelled with a code number rather than a name or initials, and accessed via a password- and firewall-protected server.

The keys linking personal details to the codes used to label other research data may be kept in paper format in lockable filing cabinets with access only by the researchers, or in a password protected spreadsheet on University approved servers. The keys should be kept separately from other study data. Such keys should be destroyed as soon as no longer needed, as should other personal data (with due regard to University and other guidelines on data retention, e.g. of consent forms).

Contact details may be retained after the end of the research where the participant agrees to be contacted for future studies. These should be held separately from the study data, and a copy of the consent form retained as evidence of agreement to be contacted. For participants who do not wish to be contacted in the future, contact details will be destroyed as soon as possible after completion of their research participation. Personal and research data may be viewed by regulatory bodies and designated individuals within the University of Oxford for the purposes of monitoring and auditing the research with the written consent of the participant.

Anonymised data may be shared with other research institutions, including researchers outside of the UK and the EU, for use in other and future research studies. For detail on anonymisation, please refer to the Information Commissioner's Office (ICO) Code of Practice –'Anonymisation: managing data protection risk', especially Appendix 2 and Annex 1.

Where data has been anonymised (all identifying information removed, including any linkage document), there is no limit as to how long this may be retained by the researchers. However, the period of retention should be stated on participant information.

Sharing of Data

Research teams will be encouraged to make their data available for reuse and validation. In all cases, the data will be shared as openly as possible and as closed as necessary in order to protect the privacy of participants. Online repositories will be assessed by research teams for their appropriateness with regard to:

- the required treatment and de-identification of unique brain and biometric data in line with UK GDPR;
- control of how the data are accessed and re-used, including terms to protect the ongoing privacy of participants;
- required attribution of the data to the originating research team, the University and funding bodies;
- management of data withdrawal requests made by participants.

11. CHANGE HISTORY

Version No.	Significant Changes	Previous Version No.
1.0	Retitled 'Approved Procedure' (previously 'Protocol'). Approved by CUREC, 19 November 2015	N/A
2.0	Quinquennial review and update	1.0
2.1	Removed reference to associated information sheet and consent form	2.0
3.0	Removed EEG and MEG, referring instead to the specific procedures for these recordings, and stating that this procedure may be combined with either the Approved Procedure for EEG or that for MEG. Updated section on training of research staff.	2.1
3.1	Updated hyperlinks for new CUREC website	3.0
3.2	Text to indicate procedure may be combined with AP20	3.1
4.0	Incorporated Approved Procedure 10 (Functional Transcranial Doppler Ultrasonography to Measure Cerebral Lateralisation in Adult Volunteers) Incorporated Approved Procedure 14 (Recording of Electrodermal Responses (Skin Conductance) from the Hand) Added high-resolution retinal imaging with the AO-SLO	3.2
4.1	Updated to improve accessibility	4.0
4.2	Removed reference to AP20 (retired procedure) Administrative revisions Complete update of data management section - text approved by CUREC Nov 2021	4.1
5.0	Quinquennial review Revised to clarify training requirements Clarification of adverse event reporting Added reference to adaptive optics optical coherence tomography (AO-OCT) Included use of dilating eye drops for advanced retinal imaging	4.2

APPENDIX A - RECORDING OF ELECTRODERMAL RESPONSES (SKIN CONDUCTANCE) FROM THE HAND

The Skin Conductance Recording (SCR) provides a measure of changes in the electrical conductance or resistance of the skin that originate primarily from movement of sweat within the eccrine sweat ducts. SCR fluctuates spontaneously and also in response to the presentation of stimuli which are novel, unexpected or significant, or by the omission of an expected response. A basic distinction can be made between tonic and phasic SCR. Phasic SCR refers to changes in SCR (increases or decreases in resistance/conductance) that are superimposed on a background – tonic – level of activity. SCR can be quantified in several ways. Sometimes researchers will be interested in spontaneous fluctuations in SCR (non-specific skin conductance responses – NS-SCR) whilst at other times they will be interested in changes in skin conductance in response to the presentation of particular stimuli or the participant's conduct of particular activities (event-related SCR – ER-SCR).

A number of measurements of SCR can be derived. These include *frequency* over a particular recording period, *amplitude* (the mean amplitude averaged across trials where an ER-SCR is observed) and *magnitude* (the mean maximum amplitude averaged across all trials). These measures are derived through off-line analysis of data collected during sessions. Usually a latency window of 1-4 seconds post-stimulus presentation is employed in order to identify skin conductance responses that are likely to originate from the stimulus presentation. On some occasions a longer post-stimulus window may be utilised, depending on the nature of the stimulus.
In experimental paradigms, the SCR is usually recorded whilst people view stimuli, perform cognitive tasks or sit at rest. Recording of the SCR is achieved by measurement of current flow between two electrodes placed on the skin of the fingers or palm (see below for precise locations). A constant voltage is maintained between the two electrodes such that current flow reflects the reciprocal of skin resistance.

Electrode placement and preparation should typically take no more than 5 minutes. The participant is asked to wash their hands with a non-abrasive soap prior to electrode placement. Depending on the set-up employed, two electrodes will then be attached to either the volar surfaces of the medial phalanges, the volar surfaces of the distal phalanges or thenar and hypothenar eminences of the palms. Electrodes are usually attached to the non-dominant hand since this is less likely to be affected by cuts or callouses and since this leaves the dominant hand free to make responses (e.g. button presses). Silver-silver chloride cup electrodes are typically used. In order to establish electrical contact between the skin surface and the electrodes, a unibase electrolyte paste is inserted into the cup electrodes, which can be attached to the skin surface either using double-sided adhesive collars, or in some custom made systems via specially designed Velcro pouches.

Usually after the electrodes have been applied the participant will be asked to sit at rest for a few minutes to stabilise SCR activity before beginning cognitive tasks.

APPENDIX B – FUNCTIONAL TRANSCRANIAL DOPPLER ULTRASONOGRAPHY

Functional transcranial Doppler ultrasonography (fTCD) is a non-invasive method of measuring cerebral blood flow that has been used in research contexts to assess cerebral lateralisation since the early 1990s.

Cerebral blood flow velocities in the supplying arteries increase with neural activation in the corresponding brain region. Blood flow velocities in the middle cerebral arteries can be measured by transcranial Doppler ultrasonography using the Doppler Effect. An ultrasound signal directed at a blood vessel is reflected and back-scattered from moving objects (e.g. blood cells) with a positive or negative frequency shift. The faster the blood cells are moving, the higher the Doppler shift.

Doppler probes are mounted on the left and right sides of the head, just in front of the ears, with an angle of approximately 90 degrees to the direction of blood flow. A small amount of conductive gel is applied between the probes and the skin. The probes emit ultrasound with a given wavelength, which is reflected back with a shortened wavelength (Doppler shift). From the degree of shift one can compute blood flow velocity. The angle of the probe is adjusted to get the best signal. Because the insonation angle is not precisely known, measures of absolute blood flow are not very reliable. However, relative changes in flow in the two sides can be more reliably measured, and have been shown to provide a good index of cerebral lateralisation for speech, with excellent agreement with more invasive procedures (e.g., the Wada test, where a barbiturate is injected into the bloodstream to temporarily 'shut down' one cerebral hemisphere).

APPENDIX C - HIGH-RESOLUTION RETINAL IMAGING WITH AN ADAPTIVE OPTICS ENABLED INSTRUMENT (AO-SLO OR AO-OCT)

Whilst low-resolution images of the human retina (the light sensitive tissue at the back of the eye) can be obtained routinely in optometry and ophthalmology clinics, the image quality is limited by the relatively poor optics of the eye, so that small features such as individual photoreceptors – rod and cone cells – are not resolved. Adaptive Optics (AO) imaging systems measure optical distortions and compensate for them. Thus, AO retinal imaging systems (such as the adaptive optics scanning laser ophthalmoscope (AO-SLO) and the adaptive optics optical coherence tomography (AO-OCT)) allow visualisation of individual cells (< 4 µm) in the living human eye, and are revolutionising our understanding of functional vision, both in health and in disease. Additionally, the scanning nature of the AO-SLO allows for highly accurate eye-tracking, beyond that capable of research-grade eye-trackers that are based on reflection from the front surface of the eye.

Researchers will typically use a dental impression to help stabilise head position, made from a resin-based compound often used by dentists. Impressions will be made for each participant and will be destroyed on the participant's last imaging session. Minimising head motion is particularly important when a video-based eye-tracker is to be used simultaneously with the AO-SLO and for some specific psychophysical experiments. In other cases, if a good level of stability can be maintained with a chin rest, a dental impression may not be required.

As is common in optometry and ophthalmology clinics, eye drops may be used to dilate the pupil and improve the quality of the retinal images. For this purpose, Tropicamide eye drops will be used, since they are fast acting and short-lived. Eye drops will be administered by trained researchers. Even if the researcher is not clinically qualified, they will be able to administer the eye drops as long as they have been trained and demonstrated competency to the required standard. This competency must be documented before they begin. If the participant has had dilating eye drops put into their eyes, they may find that the drops blur their vision and make them sensitive to light. For the participant's safety and that of others they must not drive or cycle, and must not use tools or machines, for six hours after the drops have been administered.

Before collecting retinal images, the power at the eye-piece must be checked with a power-meter. In current operation of the AO-SLO (October 2024), this level is expected to be below 140 µW, which is well below (<20%) of the maximum permissible exposure (MPE). Only after the power level at the eye has been confirmed, will the participant be invited to look into the system.

During imaging, a tiny spot of light will be scanned over a small patch of the participant's retina (a patch with angular extent of about 1.0° by 1.6°, corresponding to approx. 300 µm by 480 µm on the retinal surface).

Safety calculations of light exposure are performed for worst-case scenarios. The Maximum Permissible Exposure (MPE) from the viewing position based on 8.3 hours continuous viewing (and incorporating the field sizes and wavelengths to be used) has been calculated, and the maximum corneal exposure is <20% MPE. In practice, the corneal exposure is kept to the minimum required to obtain good images, which is typically <12.5% MPE, and viewing will not be continuous as imaging will take place in short bursts of a few minutes with breaks in between.

As at October 2024, the AO-SLO is not used for research with children.