Non-Invasive Magnetic Resonance Imaging (MRI) Investigations in Research Participants

1. Notes

This Approved Procedure can be combined with Approved Procedure CUREC_AP_IDREC_03 "Studies Involving Electrophysiological Recordings from the Scalp in Adult Participants" to conduct MRI and EEG simultaneously.

2. Scope

Magnetic Resonance Imaging (MRI) can be used to measure the structure and function of the brain and nervous system. While there are some risks associated with scanning some participants (such as those with certain implants), these risks can be reduced when proper safety procedures are followed.

This Approved Procedure is intended for use when:

- Imaging will be of the brain, central nervous system (CNS) or peripheral nervous system (PNS)
- The research involves only participants who are not recruited via the NHS*.
- no licensed drug or other (non-drug) substance will be administered
- There will be no specific brain stimulation (e.g., TMS, DCS) at the same time as MRI

**Note that under 18-year-olds may be scanned for research under this procedure only where specific consent is provided by their parent/guardian. Should you wish to scan 16–18-year-olds without parental consent, you must justify the reasons you do not intend to obtain parental/guardian consent on your application, and full committee review of the application will be required.*

This Approved Procedure can be used on any scanner that is owned and managed by the University of Oxford, including:

- The 3 Tesla (3T) and 7 Tesla (7T) MRI scanners in the FMRIB Building (Wellcome Centre for Integrative Neuroimaging)
- The 3 Tesla MRI scanner at OHBA (Department of Psychiatry)
- The 3 Tesla and 1.5 Tesla MRI scanners at OCMR (Division of Cardiovascular Medicine)

3. Specific procedures

Research covered by this Approved Procedure may involve characterisation of the basic structures, physiology and biochemistry of the CNS and PNS using MRI techniques including:

- Structural measures using contrasts based on proton density, relaxation times, magnetisation transfer, susceptibility or diffusion

- Connectivity measures using diffusion-based MRI contrast (DTI)
- Task-related and resting functional MRI (fMRI)
- Perfusion based MRI measurements (ASL)
- Magnetic Resonance Spectroscopy (MRS)
- One or more scanning session (of no more than 2 hours each session)

MRI compatible measurement of physiological signals (pulse, respiration, pupil dilation, eye movement) can be digitally recorded.

Electroencephalogram (EEG) signals can be recorded simultaneously with MRI by combining this Approved Procedure with CUREC_Approved_Procedure_IDREC_03, provided a specialised MRI-compatible EEG cap is used.

When the participant is required to carry out a task, they can be presented in one or more of the following ways:

- sensory stimuli delivered through MRI compatible headphones (or similar), on a screen or by touch
- texture or temperature change applied to the skin in a safe way
- spoken or written language (words or passages) presented visually or aurally
- tastes or smell delivered through MRI compatible systems
- pictures and drawings, including faces, depicting emotional or non-emotional scenes

The participant may respond using

- simple motor movement including responses using an MRI compatible button box, pressure-pad or joystick
- repetitive movements of parts of the body (e.g., fingers or foot)
- vocalisations
- eye movement measured by MRI-compatible eye-tracking system
- vocalised responses recorded using audio equipment

Some participants may be asked to solve reasoning problems presented visually or verbally either with or without simple reinforcements (including small amounts of money).
Importantly, these defined types of studies should have little associated hazard or discomfort for the participants. In studies where stimuli have explicit emotional valence, participant information sheets need to give appropriate details. If there is significant risk that that the stimuli are of a level or type that could have short- or long-term harmful physical effects or will induce anxiety, stress or other harmful psychological states in participants that might persist beyond the duration of their involvement in the research, full committee review of the application will be required.

Cognitive and performance measurements may be acquired outside of the scanner, during scanning, or both, in testing sessions lasting about 30 minutes to two hours. The maximum time to be spent in a session in the scanner room will be two hours; if MRI scanning is accompanied by other tests, participants must be allowed to take at least 30 minutes' break between test procedures. A participant may therefore be at the Centre for an entire morning/afternoon, depending on the research. Questionnaires other than the MRI safety form, if used, will be detailed in the application.

4. Training of research staff

In addition to the training expectations for carrying out research on human participants (such as Ethics and Integrity training (mandatory), Good Clinical Practice (optional), information security and

data privacy awareness training), all researchers are required to complete annual MRI safety training – failure to undergo this training will involve revocation of access to the Centres.
All scanning will be conducted by a fully trained MRI operator or Health and Care Professions Council (HCPC) registered radiographer.

5. Methods for recruiting participants

Potential participants will usually be identified by poster adverts, social media, word-of-mouth, e-mail postings to departmental and college mailing lists and online participant recruitment systems (e.g. SONA).

Recruitment material must contain:

- Study title
- Ethics reference
- Department details
- Brief description of research including what they would have to do, number of sessions, duration of each session, location and inclusion/exclusion criteria

A generic advert template is available on the CUREC website, and all adverts used (including emails) must be approved as part of the ethics review process. When a potential participant registers interest, further information (prepared using the associated template information sheet) will be provided, together with details as to how to confirm they would like to take part.

6. Information provided to participants

All information provided should be appropriate to the specific research and presented in an accessible way. If there is not enough information, potential participants might not be able to make an informed decision. On the other hand, if the information sheet is too long or unclear (e.g., through using overly technical language), they might not read it properly or it could deter them from taking part. 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.

Specific statements relevant to MRI will include:

- the procedure for dealing with incidental findings
- MRI risks, and preparation procedures – removal of make-up, changing into scrubs, metal impregnated clothing etc.
- the de-identification procedure you will follow to prepare data for open sharing, and the protection of the participant's privacy in shared data.

Please refer to, and use, the **Information Sheet associated with this Approved Procedure**.

7. Consent of participants

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

Consent will be obtained by a member of the research team who has appropriate training, as confirmed by the Principal Investigator. Vulnerable populations or participants who are unable to provide informed consent will be excluded.

Specific statements relevant to MRI will include:

- Statement about incidental findings and that participants will only be informed if a doctor thinks it is medically important
- Brain images that leave the Centre will be de-identified

8. 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 offer a performance-related reward. Individual research proposals will detail the value (if any) of compensation to be offered. Compensation is limited to the time and inconvenience incurred as well as reasonable travel expenses and will in 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.

9. MRI safety screening

Before attending the Centre for their scan, participants will be sent a copy of the MRI safety screening form or called by the researcher to go through the form over the phone. If the participant answers 'YES' to any of the questions on the form, the researcher will seek advice from the Centre's written safety procedures or contact the staff listed in these procedures for advice.

On the day of the scan, the participant will be screened once again by the radiographer or trained MRI operator, who will make the final decision on whether to scan.

10. Potential risks to participants/researchers/others and what will be done to minimise these

Comfort

MRI scans can be very noisy, so participants will be given suitable hearing protection (usually ear plugs) to bring the sound to a safe level. If auditory stimuli are being presented, then MRI compatible ear or headphones will be used. Should the researcher need to be in the MRI scan room during scanning, they will also wear hearing protection.

The enclosed space of the scanner can induce feelings of claustrophobia. All operators and radiographers are trained to dealing with participants who may be claustrophobic and have a variety of strategies to employ with people who exhibit feelings of claustrophobia, but who still wish to participate in research. Participants will be introduced carefully to the scanner and allowed to leave at any stage. Whilst in the scanner, participants have easy access to a call button should they wish to stop the scan or speak with the radiographer or operator. Angled mirrors enable the participant to see outside of the scanner or to view stimuli presented on a screen.

During scans, participants are asked to lie still on their back. Lying on the scanner table for prolonged times can induce temporary lower back pain. MRI-compatible pads and cushions are used to improve participant comfort.

Metal objects

Ferromagnetic metal objects will be attracted to the magnet with significant force. Other conductive metal objects (e.g., an implant that the participant may have) have the potential to heat during scanning. Whether it heats will depend on the size and shape of the object and its location within the transmit radiofrequency (RF) field of the scanner.

Participants will be screened for surgical or other implanted metallic devices as a result of surgery or accidents every time they attend for a scan. The safety to scan any devices identified will be ascertained using established centre procedures. If it is not clear that that it is safe, then the participant will not be scanned. To minimise the risk of ferromagnetic objects or other unsafe objects being on the persons clothing, participants will be changed into pocket-less surgical scrubs for their scan.

Researchers are safety screened on a yearly basis and asked to screen again should their circumstances change. The yearly magnet safety training reminds researchers of the risks posed by ferromagnetic objects being taking into the magnet room. No ferromagnetic objects are taken into the magnet room unless a risk assessment has been carried out and written equipment protocol produced. No conductive objects are used within the transmit RF field during scanning unless a risk assessment has been carried out and written equipment protocol produced.

Tattoos

Participants with tattoos will be warned of the rare complication of heating and to inform the radiographer or scan operator immediately if they feel any heating.

Participants with new tattoos will not be scanned until 48 hours after to avoid the risk of smearing or blurring.

On the 7 Tesla MRI scanner, participants with tattoos that lie within the transmit RF field will be excluded from scanning. This is determined in the first instance by whether the tattoo is within 35 cm of the top of the head. Tattoos on the shoulder or that are borderline will be evaluated on a case-by-case basis depending on the exact location of the tattoo relative to the transmit RF field. Participants with tattoos outside of this, and where scanning is allowed, will be warned of the rare complication of heating and to inform the radiographer or scan operator immediately if they feel any heating.

Dizziness on going into or moving out of the scanner (7 Tesla MRI only)

Participants moving in to or out of the very high magnetic field of the 7 Tesla MRI scanner may experience various effects including dizziness, nausea, magnetophosphenes (which can be perceived as flashes of coloured light) and a metallic taste in the mouth. These effects are transitory and usually stop as soon as the participant is no longer moving. These effects are related to field strength and the speed of movement through the magnetic field. The 7T MRI system limits the speed the participant moves into the scanner, so these effects are minimised.

The information sheet and the operator will inform participants of the possibility of dizziness before they go in the scanner. If the participant does experience dizziness, the operator may choose to temporarily halt the table movement. The participant may choose to continue to the centre of the scanner where any adverse sensations will gradually resolve, or they may choose to stop all procedures and come out of the scanner (either temporarily or to withdraw altogether).

On the rare occasion where the effects last beyond the person being removed from the scanner (an effect similar to motion sickness), the researcher will wait with the participant until they feel able to leave.

Combined MRI and EEG

EEG equipment to be used in conjunction with MRI scans will be in all cases certified as 'MR conditional' up to the field strength being used in the research (e.g., 3 Tesla).
During the session, participants are asked to indicate if they feel any discomfort, in which case the procedure is stopped.

See Approved Procedure CUREC_AP_IDREC_03 "Studies Involving Electrophysiological Recordings from the Scalp in Adult Participants" for additional risks and mitigations specific to the EEG recording.

Infection Control

Infection control measures are in place at WIN and the degree of these measures may vary depending on the level of risk presented at the time. Individual researchers should complete a risk assessment for their project if there are particular concerns with their research population and/or research team regarding risk of infection.

11. Monitoring and reporting of adverse or unforeseen events

In the event of an emergency incident, the emergency response team in the adjacent John Radcliffe Hospital covers FMRIB and OCMR. Emergency supplies (e.g., defibrillator) are available on site. For OHBA, researchers should telephone 999 as there is no emergency response team on the Warneford site.

Any safety incident or near miss should be reported to the local staff and recorded on the University Incident Reporting Form so that it can be reviewed by the appropriate Department safety committees.

Any serious adverse event related (resulted from administration of any of the research procedures) and unexpected (the type of event is not listed as an expected occurrence) should be reported to the Research Ethics Committee as soon as possible once the Principal Investigator becomes aware of the event.

12. Communication of results

Graphical Representations

Results may be written up for publication in peer-reviewed scientific journals, presented at scientific conferences (in abstract or presentation formats), submitted as part of course degrees and may form part of grant applications. Data from multiple participants will be combined such that individual participant data is not represented. Where it is preferable to present data from a single participant (for example as an indicative response), care will be taken to prevent identification of the individual (e.g., presented in normalised brain space or restricted field of view).

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.

13. Management of incidental findings

Occasionally, MRI studies identify abnormal anatomy or pathology in otherwise apparently healthy participants. If an abnormality is detected, the Centre's SOP "Dealing with Neuro-Incidental Findings" will be followed. The Principal Investigator would alert the Contact Radiographer who will make an initial assessment as to whether the abnormality may reflect a scanner artefact or is of a trivial nature. Once an incidental finding is suspected, the Contact Radiographer will inform the Contact Clinician as soon as possible, who will meet with the Contact Radiologist at the John Radcliffe Hospital and together decide whether the finding warrants further clinical investigation. In this eventuality, the Contact Clinician would contact the participant directly and the appropriate action be discussed. The Contact Neurologist maintains a database with anonymised summary information on the outcomes of all referrals.

Some studies may use validated questionnaires asking participants about state and trait anxiety and/or depression to interpret how these factors influence processing and perception of research stimuli. These questionnaires are not used for recruitment or screening purposes. However, if a researcher, as a result of these questionnaires, has concerns that a participant may have an undiagnosed psychiatric condition that is causing distress, CUREC guidance (BPG08) will be followed. The researcher will seek advice from the Principal Investigator who may discuss the symptoms in greater detail with the participant and/or offer the opportunity to speak with a senior clinical researcher if they are not clinically trained themselves.

14. Data management and protection

The research must be conducted in accordance with the University's 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.

Authorised scanning centre personnel and investigators listed as being on the research team will have access to the MRI data. MRI data is automatically coded at source and stored with a unique key in a secure database within the scanning system. Such data thus retains a link to direct identifiers within the scanning system, even after destruction of research study personal data. Imaging data held by scanning facilities will be stored on archive tapes indefinitely, even if the participant withdraws from the research they are enrolled in, and this must be explained to participants when obtaining their informed consent for data collection and retention. 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. Any other data where there remains a link to identifiers outside the control of the research team should be set out in the information sheet.

Personal information held by the research team (such as contact details, consent forms and screening forms) 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. 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. 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 their 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. This includes MRI scan data because, although a copy of the scan is archived in the scanning system in a form linked to identifiers, this archived copy will not be linked to the data shared with other researchers for secondary use. Removal of the MRI code is part of anonymisation required before research data is shared. See https://ico.org.uk/media/1061/anonymisation-code.pdf especially appendix 2 and annex 1 for detail on anonymisation.

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.

In completion of the online application, the following statements about MRI scan data should be included in the data management tab:

Please describe the procedures to be used to ensure confidentiality of data both during the conduct of the research and in the release of its findings.

Response: Imaging data is automatically coded at source with a scan identifier that cannot be directly linked to the participant by anyone outside of the centre where the data was acquired.

How will access to the data be controlled?

Please describe arrangements for physical and technical security measures. This may include (but is not limited to) access controls in work spaces, use of encrypted devices, password protected documents or controlling editing rights on shared documents

Response: Imaging data is only accessible by researchers working on this research and authorised centre staff.

How long will the data be retained after the project is complete?

Please advise the latest data storage end-date for each type of data collected. Refer to institutional retention schedules and funder requirements

Response: The scan identifier and imaging data will be stored on secure University managed IT systems, with participant name encrypted. The data will be stored indefinitely.

15. Further information and documents

AP17 Consent form

AP17 Participant Information Sheet

Standard Operating Procedures (SOPs) for MRI scanning

SOP "Dealing with Neuro-Incidental Findings"

3T Volunteer MRI safety screening form

7T Volunteer MRI safety screening form

University Incident Reporting form

16. Change History

Version Number	Significant Changes	Previous Version Number
3.0	Incorporates reference to the University Safeguarding Code of Practice and related requirements. Retitled `Approved Procedure' (previously 'Protocol'). Approved by CUREC, 19 November 2015	N/A
4.0	Removed requirement of study documents to be reviewed by CTRG prior to submission to the relevant IDREC	3.0
5.0	Changes made to reflect current processes at University scanning sites	4.0
6.0	Change of site name from the Oxford Centre for Functional Magnetic Resonance Imaging of the Brain (FMRIB) to the Wellcome Centre for Integrative Neuroimaging (WIN) Removal of statement that previously excluded claustrophobic participants from taking part	5.0
6.1	Added a statement to say this procedure can be combined with AP02 (EEG)	6.0
6.2	Updated to improve accessibility	6.1
6.3	Revision to section 11 to include current information about storage of, and access to, Imaging data	6.2
7.0	Complete re-write to reflect current practices and remove description of MRI. Updated Data Management section.	6.3
7.1	Clarification of timescale for reporting adverse events	7.0
7.2	Replace reference to centre databases with 'University managed IT systems'	7.1
7.3	Addition of text to section 10 about infection control	7.2
7.4	Added reference to Worktribe Ethics online application system	7.3

Version Number	Significant Changes	Previous Version Number
8.0	Information about reporting of adverse events updated (section 11) Whole document revised to reflect implementation of online ethics application system	7.4