The "OMEGAMIND" study

OPM- **MEG** in non-immune **A**nd i**M**mune-med**I**ated **N**eurological **D**isease

PROTOCOL VERSION AND DATE

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KEY STUDY CONTACTS

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ABBREVIATIONS

BRIEF – Behaviour Rating Inventory of Executive Function

CBCL – Child Behaviour Checklist

DWI – Diffusion Weighted Imaging

fMRI – Functional MRI

PedsQoL – Paediatric Quality of Life

SDSC – Sleep Disturbance Scale for Children

SDQ – Strengths and Difficulties Questionnaire

T1W – T1 Weighted Imaging

WPPSI-4 – Wechsler Preschool and Primary Scale of Intelligence, 4th Edition

WISC-5 – Wechsler Intelligence Scale for Children, 5th Edition

WIAT-3 – Wechsler Individual Achievement Test, 3rd Edition

ABAS-III – Adaptive Behavior Assessment System, 3rd Edition

AE – Autoimmune Encephalitis

ADEM – Acute Disseminated Encephalomyelitis

MS – Multiple Sclerosis

MEG – Magnetoencephalography

OPM-MEG – Optically Pumped Magnetometer – Magnetoencephalography

IHN – Institute of Health and Neurodevelopment

BCH – Birmingham Children's Hospital

REC – Research Ethics Committee

PPIE – Patient and Public Involvement and Engagement

STUDY SUMMARY

Trial title	**The "O-MEG-A-MIND" study: OPM- MEG in non-immune And iMmune-medIated Neurological Disease**	
Study design	**Basic science study procedures with human participants**	
Study participants	**Paediatric patients with non-immune and immune-mediated neurological disease**	
Planned sample size	**75**	
Duration	**8 years**	
Planned study period	**2026 to 2034**	
	Objectives	**Outcome measures**
Primary	To use advanced magnetoencephalography with optically pumped magnetometers (OPM-MEG) to develop non-invasive measures of brain dysfunction of clinical relevance in children and young people with immune- and non-immune mediated neurological disease.	Detection of group differences over time in imaging metrics using OPM-MEG.
Secondary	To assess standard MEG and MRI measurements at the same time-points.	Detection of group differences over time in imaging metrics using MEG and MRI.
	Explore relationship between cognitive, behavioural and functional outcomes and OPM-MEG, MEG and MRI imaging metrics.	Assess use of imaging metrics as clinical predictors of disease outcome.

FUNDING AND IN-KIND SUPPORT

FUNDER(S)	FINANCIAL AND NON-FINANCIAL SUPPORT GIVEN
Wellcome	Staffing and scan costs
Aston University	In-kind staff and scan costs

ROLES AND RESPONSIBILITIES OF STUDY MANAGEMENT COMMITEES/GROUPS & INDIVIDUALS

Sukhvir Wright has overall responsibility for the running of the study. She will by supported by a funded research team consisting of post-doctoral researchers, an academic clinical fellow and PhD students. Professor Wright will have a Steering Committee in place to provide overall guidance for the study. As per NIHR research governance guidelines, they will provide advice, monitor progress, and most importantly ensure the study team uphold the rights, safety and well-being of our participants. NIHR guidelines will be followed for reimbursement of costs/time when indicated (for lay members). Meetings will be 6 monthly in the first 3 years then move to annually.

Membership of Steering Committee:

- Mr Satnam Bains: Expert by experience (parent of patient with autoimmune encephalitis), professional interest in digital health.
- Encephalitis International: one member from this charity will be on the committee.
- SHAPE network: two members from the SHAPE network will be on the committee. This network is the largest PPIE body interested in epilepsy and part of the Epilepsy Research Institute UK.
- Professor Ming Lim: Expert in Childhood CNS Neuroimmunology at Evelina Children's Hospital
- Emeritus Professor Stefano Seri: Expert neurophysiologist with extensive experience in MEG, fMRI
- Rachel Satodia: Young person with interest in medicine, advocate for the young people in the study.
- Dr Laavanya Damordaran: Consultant Liaison Psychiatrist, BCH

KEY WORDS: Autoimmune encephalitis, ADEM, MOG, MS, OPM-MEG, MEG, neurodevelopment, neuropsychology

STUDY SUMMARY

Abstract: Recognition and treatment of immune-mediated neurological disease has dramatically increased over the past 20 years. The most common immune-mediated neurological disorders include autoimmune encephalitis, acute disseminated encephalomyelitis (ADEM) and multiple sclerosis. Despite advances in recognition and treatment of these disorders, outcomes remain static, and children are disproportionately poorly affected. MRI scans and other outcome measures do not accurately demonstrate the high incidence of comorbidities we see including neuropsychiatric symptoms, cognitive decline, sleep difficulties and lack of prosocial behaviours. In our preliminary brain network studies using magnetoencephalography (MEG) we captured specific network alterations in these patients which correlated with lower working memory. This study will leverage cutting edge optically pumped magnetometers to measure brain network alterations from children as young as 2 years with immune-mediated neurological diseases, demonstrate feasibility and compare to changes seen in non-immune mediated neurological disease. In the longer term, we aim to prove this technology's benefit to neurological patients of all ages in terms of outcome prediction and biomarker discovery.

Lay summary: Over the past 20 years, doctors have gotten much better at spotting and treating brain conditions caused by the immune system attacking the body. These include illnesses like autoimmune encephalitis, ADEM, and multiple sclerosis. But even with better treatments, many patients—especially children—still struggle with long-term problems. Standard brain scans and tests often miss important issues like memory problems, emotional difficulties, trouble sleeping, and challenges with social behaviour. Early research using a special brain imaging technique (called MEG) has shown changes in brain networks that seem to be linked to poor memory. This study will use a new, advanced version of MEG that works even with very young children (as young as 2 years old). The goal is to better understand how these brain conditions affect children, compare them with other types of brain illness, and eventually use this technology to help predict outcomes and discover new ways to track brain health.

TABLE OF CONTENTS

BACKGROUND 9

Autoimmune encephalitis and ADEM 9
Multiple sclerosis 10
Rationale for use of OPM-MEG 11

STUDY AIMS 12

STUDY OUTCOMES 13

STUDY DESIGN 13

STUDY ACTIVITIES: 14

STUDY SETTING 17

PARTICIPANT ELIGIBILITY CRITERIA 18

PARTICIPANT IDENTIFICATION AND RECRUITMENT 18

CONSENT: 19

WITHDRAWAL FROM THE STUDY 21

END OF STUDY 22

ONSITE STUDY VISIT PROCEDURES 22

RISKS AND BURDENS: 25

ADVERSE EVENTS 27

STATISTICS AND DATA ANALYSIS 27

DATA MANAGEMENT PLAN 28

Consent to Data Sharing: 28
Open access: 28
Data sharing with clinical teams: 28
Participant data: 29
Clinical Report Form Data 29
MRI Data 29
Questionnaire, Neuropsychology, and demographic data 30
Data Storage 30
Data retention 30

MONITORING, AUDIT & INSPECTION 31

ETHICAL AND REGULATORY CONSIDERATIONS 32

PEER REVIEW 32

PUBLIC AND PATIENT INVOLVEMENT 32

PROTOCOL COMPLIANCE 33

FINANCIAL AND OTHER COMPETING INTERESTS FOR THE CHIEF INVESTIGATOR, PIS AT EACH SITE AND COMMITTEE MEMBERS FOR THE OVERALL STUDY MANAGEMENT 33

INDEMNITY 33

AMENDMENTS **33**
REFERENCES **34**
APPENDICES **36**

BACKGROUND

Recognition and treatment of immune-mediated neurological disease has dramatically increased over the past 20 years.[1] Any age of patient can be affected. The most common immune-mediated neurological disorders include autoimmune encephalitis, acute disseminated encephalomyelitis (ADEM) and multiple sclerosis.[2]

Autoimmune encephalitis and ADEM

Patients with autoimmune encephalitis (AE) and ADEM present with behavioural change, seizures, cognitive and sleep dysfunction, and movement disorders (AE). While we are succeeding with early diagnosis, initiation of immunotherapy and even prevention of relapses, longer-term outcomes remain frustratingly static.[3] Chronic symptoms include ongoing sleep disruption, neuropsychiatric disorders and persistent cognitive dysfunction. Children are disproportionately affected, particularly under-5yrs.[4] In our preliminary studies of paediatric AE and ADEM patients, at least 18 months after diagnosis, we have found:

• a high incidence of neuropsychiatric symptoms including emotional problems, hyperactivity, prosocial behaviours;

• patients have been classified as having a "good" outcome (modified Rankin scores (mRs) 0-2) but their ongoing difficulties are similar to those seen in other chronic diseases e.g., epilepsy and stroke;

• in structural MRI studies, local cortical thinning in brain areas where thickness has been linked to emotional difficulties and general intellectual impairment;

• in network studies, magnetoencephalography (MEG) captures specific network alterations which correlate with lower working memory [5].

The MRI and MEG changes were found in patients considered to be "recovered" and were also different to those with other neurological disease, i.e. epilepsy.

In fact, altered brain network activity is a prominent, but neglected feature of AE and ADEM, especially in children. Magnetoencephalography (MEG) provides a non-invasive measurement of functional brain dynamics that is a direct measure of neuronal activity, unlike fMRI which relies on a surrogate signal based on blood oxygenation levels. MEG can reveal widespread changes in functional connectivity with higher temporal resolution than fMRI, which is especially relevant to

examining synchrony of neural oscillations across brain regions.[6]In addition, MEG provides better spatial resolution than EEG, being less susceptible to skull bone signal distortion. MEG has already been used effectively in paediatric epilepsy to predict outcomes and is well-tolerated, cost-effective, non-invasive, and reproducible.[7-9] Longitudinal characterisation of the underlying dysconnectivity even in the youngest patients with immune-mediated neurological disease would have a huge impact on our understanding of disease course and recovery trajectory.

Multiple sclerosis

Approximately 150,000 people (including 250 children) in the UK are living with multiple sclerosis (MS), an incurable disease where immune cells attack the myelin sheaths covering nerves, resulting in demyelination and axonal damage with the central nervous system and causing blindness, paralysis and/or persistent numbness. Significant advances have been made in MS treatment using highly effective disease-modifying drugs which dramatically reduce MS relapses.[10-12] The traditional perception of MS characterised by "RAW" or relapse-associated worsening is now challenged in the field and replaced with concepts such as "PIRA" – progression independent of relapse activity – and "smouldering MS" – ongoing, subclinical neurodegeneration that occurs independently of acute relapses or new MRI-visible inflammatory lesions.[13] PIRA and smouldering MS are becoming increasingly recognised as major drivers of long-term disability in affected patients.[14] A recent study in Paediatric onset MS (POMS) found that PIRA was observed in 40.4% of POMS patients even when they were still young.[15]

Regular interval MRI brain scans (at least annually) have long been the established metric used for measuring MS disease activity but now show remarkable stability with no new MRI-visible inflammatory lesions ("NEDA" – no evidence of disease activity), in those taking high-efficacy treatments. This limits the use of MRI as a continued biomarker in this population. Despite achieving radiological NEDA, MS patients still experience symptoms of fatigue, memory, mood and concentration difficulties significantly affecting their quality of life. For example, on surveying our paediatric-MS patients annually (2024, n=18; 2025, n=12), >80% of patients with NEDA on MRI still suffer with MS symptoms, at least 50% have memory problems and up to 60% suffer with symptoms of anxiety and depression. In children with MS, these symptoms can lead to lower educational achievements, lower employment and earnings, and greater reliance on disability benefits in adulthood.[16]

In the context of MS, brain network measures using MEG have the potential to serve as powerful paraclinical biomarkers and improve our understanding of the clinical-radiological paradox of why MS patients are suffering with symptoms despite consistent MRI brain scan stability. MEG has been employed as a research tool by us and others in MS and other neuroinflammatory diseases for detection of cognitive impairment and assessment of functional connectivity identifying changes in neural activity not apparent on conventional MRI.[5, 17, 18]

This demonstrates the feasibility of MEG and provides preliminary supporting data of the link between brain network measures and cognitive outcomes in immune-mediated neurological diseases.

Rationale for use of OPM-MEG

Despite this previous research and promise of useful clinical application, MEG has not yet made it to the clinic due to the challenges of constructing a system that meets the complex physical, engineering, restrictive and high-finance requirements for optimal scanning. The advance of optically pumped magnetometers (OPMs) has the potential to revolutionise the accessibility of MEG technology for clinical use by nature of its wearable design, which enables sensors to be placed closer to the scalp in younger children, increasing signal to noise ratio for small heads where sensors would otherwise be further from the brain.[19] It also allows for participant movement during scanning. OPM-MEG offers a reproducible disease assessment tool that can be employed across the lifespan, without the need for sedation or general anaesthetic, delivering a significant shift in our understanding of immune-mediated neurological disorders like MS and AE, as well as non-immune disorders like epilepsy.

Optically pumped magnetometers (OPM-MEG) at Aston-Birmingham Children's Hospital (BCH)

Our recently installed MRC-funded Mag4Health 96 channel OPM-MEG system incorporates ^{4}Helium sensors that operate entirely at room temperature, minimising discomfort for patients of all ages. Sensors can therefore be placed directly against the scalp with an elasticated cap that moves with the patients thus allowing for excellent signal-to-noise ratio in a variety of head sizes (we have caps in development for patients from age 2 upwards). The Institute of Health and Neurodevelopment (IHN) where the system is located is a CQC-registered day hospital environment and home to the existing Wellcome Trust laboratory for MEG studies housing a cryogenic MEGIN device, as well as a 3T Siemens Prisma MRI scanner. Facilitating translation of OPM-MEG technology to the clinic was of paramount importance when designing our system. Our OPM is the only one in the West Midlands region housed in a hospital environment suitable

for patient work and supported by clinically qualified staff (Daisie Pakenham – jointly funded by Aston and BCH).

The short-term aims of O-MEGAMIND are to use OPM-MEG to characterise brain network changes in patients with immune-mediated neurological diseases and compare to changes seen in non-immune mediated neurological disease. In the longer term, we aim to prove this technology's benefit to neurological patients in terms of outcome prediction and biomarker discovery.

OPM-MEG has the potential to provide a much more ergonomic, comfortable recording experience in an environment where patients can move instead of being restricted whilst collection of functional brain activity takes place. The helmet housing the sensors can be easily adjusted to fit participants of all ages, meaning that we can, for the first time, record brain activity in awake patients from as young as 2 years. Finally, OPM-MEG systems are much cheaper to run than traditional MEG systems as they do not require cryogenic cooling and therefore potentially more cost-effective. In summary, OPM-MEG has the potential to benefit a much greater number of patients with neurological disease, transform our understanding of these diseases and improve long-term outcomes.

Study Aims

The overarching study aim is to demonstrate eventual clinical application of OPM-MEG technology in patients living with neurological disease. This requires measurement of functional brain activity to precisely monitor disease progression and predict outcomes. We hope to enable healthcare professionals to identify individuals at risk of disease progression/poor outcome, monitor treatment response and initiate therapeutic or rehabilitative interventions early to prevent poor long-term outcomes.

More specifically, we aim to:

1. Use advanced magnetoencephalography with optically pumped magnetometers (OPM-MEG) to develop non-invasive measures of brain dysfunction in children and young people with immune- and non-immune mediated neurological disease over the course of disease recovery.
2. Assess standard MEG and MRI measurements at the same time-points.
3. Explore the relationship between cognitive, behavioural and functional outcomes and OPM-MEG, MEG and MRI imaging metrics.

Study Outcomes

1. Detection of group differences over time in imaging metrics using OPM-MEG.
2. Detection of group differences over time in imaging metrics using MEG and MRI.
3. Assess use of imaging metrics as predictors of disease outcome.

Study Design

This is an 8-year cross-sectional and longitudinal prospective repeated measures observational study. The cross-sectional cohort will be 25 participants with immune-mediated neurological disease at least 18 months after diagnosis. These participants (n=25) have one study visit (study visit 1). The longitudinal cohort will be those with immune and non-immune mediated disease within 9 months of diagnosis (n=25 in each group, total n=50). They will be invited for three study visits: initial recruitment (study visit 1), one at two years (study visit 2) and one at 5 years (study visit 3). The study design is summarised in the table below:

Timepoint	Study Visit 1 Recruitment	Study Visit 2 2 years	Study Visit 3 5 years
Research activity	Demographics		
	Questionnaires	Questionnaires	Questionnaires
	OPM-MEG	OPM-MEG	OPM-MEG
	MEG	MEG	MEG
	MRI	MRI	MRI
	Neuropsychology		
Time taken (hours)	5	3	3

Table 1. Study design and visit schedule.

Study activities:

1. Demographics

   Demographic data will be collected on a paper-based form at recruitment during study visit 1 (Appendix 22).

2. Questionnaires

   To assess the behavioural and functional changes following disease from the patient and caregiver perspective the following questionnaires will be completed on paper-based forms. These are all established outcomes measures used in our and others' previous studies in immune and non-immune mediated disease in children:

   i) Strengths and Difficulties Questionnaire (SDQ): The SDQ is a brief behavioural screening questionnaire about 3-16 year olds, including subscales for emotional symptoms, conduct problems, hyperactivity/inattention, peer relationship problems, and prosocial behaviour (Appendix 23)

   ii) Paediatric Quality of Life (QoL) Generic Core Scales Short Form: to measure generic health-related quality of life. Applicable for healthy school and community populations, as well as patient populations with acute and chronic health conditions (Appendix 24).

   iii) Paediatric QoL Multidimensional Fatigue Scale: a generic symptom-specific instrument to measure fatigue in patients with acute and chronic health conditions as well as healthy school and community populations (Appendix 25).

   iv) The Sleep Disturbance Scale for Children (SDSC): SDSC is a parent-rated measure which uses 26 items to assess the occurrence of sleep disturbances over the past 6 months of a child's life. Each item on this scale is rated on a 5-point Likert-type scale ranging from 1 to 5, with higher values reflecting higher frequency of occurrence of symptoms. The sum of scores provide an indication of total subjective sleep quality, and ranges between 26 and 130. The SDSC is validated for use in children between 6 and 16years and has been used in children with brain injury (Appendix 26).

   v) Child Behaviour Checklist (CBCL; Achenbach1991): To assess for the presence of behaviours consistent with psychopathology, we will ask parents or guardians to complete the gauge axis I (psychiatric disorders) (Appendix 27).

   vi) Behavior Rating Inventory of Executive Function (BRIEF): An assessment of executive function behaviours at home and at school for children and adolescents ages 5–18 (Appendix 28).

3. Optically pumped magnetometer (OPM) - Magnetoencephalography (MEG)

   To assess the changes in brain network function that occur in relation to immune and non-immune mediated brain disease, participants will undergo OPM-MEG recording. This will be conducted at all study visits. The recording protocol will be as follows:

   i) The participant will be asked to sit in a chair inside the recording room and wear the OPM-MEG cap, similar to stretchy bike helmet holding the sensors, with a strap under the chin. A member of the research team will remain in the room, and the accompanying adult can be in the room too. The door to the recording room will be closed, but full spoken contact with the researcher will be maintained outside the recording room, and a video link so the researchers outside can see in.

   ii) The OPM-MEG recording will begin by obtaining a ten-minute baseline or "resting-state" recording i.e., when no activity/task taking place. A video may be played during this part of the recording.

   iii) The researcher may then ask the participant to perform a task while being scanned which will involve pressing a button while looking at images on the screen. This can take up to fifteen minutes.

   iv) Once the OPM-MEG recording is complete, a digital pen (Polhemus) will be used to record the shape of their head and the positions of the OPM-MEG sensors. This process will take no longer that fifteen mins.

The time for OPM-MEG scan will be approximately 60 minutes in total to allow time for completion of safety questionnaires and to acclimatise the participant to the OPM-MEG and environment. The researcher may stop and start the recording but the overall time for recording is unlikely to exceed 30 minutes. The device is silent during recording, and the participant can adjust their position, somewhat, to remain comfortable. The participant can withdraw from the recording at any time just by asking.

4. Magnetoencephalography (MEG)

   The cryogenic MEG recording will also assess changes in brain dysfunction and will be directly comparable to the advanced OPM-MEG data. This will be conducted at all study visits. The recording protocol will be as follows:

   i) The participant will first have 5 small sensors attached to their head (placed on forehead, sides and back of head) which record where the head is in the scanner.

A digital pen, similar the that used with the OPM-MEG, will be used to record the position of these sensors and the shape of the head.

ii) They will be taken into the recording room for the MEG, be seated on a chair and moved up to ensure the top of their head is in the fixed MEG helmet. Someone can always remain with them.

v) The participant will be informed when recording has started and asked to try and keep still during the first part of the recording to obtain the ten-minute resting state recording. A video may be played during this part of the recording.

iii) If compliant, they may be asked to perform the same task they did in the OPM-MEG while being scanned.

iv) At the end of the recording, the participant is moved out of the fixed helmet and 5 head sensors removed.

The time is similar to the OPM-MEG (up to 60 minutes in total with up to 30 minutes recording time). This device is also quiet. The participant can withdraw from the recording at any time just by asking.

5. Magnetic Resonance Imaging (MRI)

   To assess the effect of disease on brain structures, participants will undergo MRI scanning at the IHN. Sedation or general anaesthesia will not be used, and the investigation will only be possible if the participant can undergo the investigation without sedation or anaesthesia.

Scanning protocol will include the following MRI sequences:

- T1w structural MRI Volume (0.9 mm iso MPRAGE, IPAT4 acceleration, 3:26 minute, acquired twice and 1mm isotropic MPRAGE IPAT2 acceleration 3:26 minute)
- T2w Darkfluid/FLAIR Volume (1mm iso T2w SPACE, 5:47 minute)
- Multi-shell diffusion weighted imaging (1.7mm iso, 60 directions, 125 volumes, 4 shells (b=300, b=650, b=1000, b=2000 (7/15/30/60 dirs per b-value respectively)), and 13 b0 volumes acquired. Protocol acquired over 5 separate scanning sequences (approximately 10 minutes total scan time)).
- BOLD data will also be acquired at rest (e.g. TR 2000, 3mm isotropic voxels; 6 minutes) to examine resting state connectivity.

The time for MRI scanning will be approximately 60 minutes to ensure time is allowed for completion of safety questionnaire (Appendix 19) and to acclimatise the participant to the scanner and environment. Whilst there are multiple scanning protocols, the sequences are

optimised for speed of acquisition, to minimize the chance of movement during a scan (ensuring image quality and useability), to allow a sequence to be repeated, if corrupted by movement, and to allow for short breaks in between sequences for our research radiographers to keep in communication with the children, to ensure they are happy and comfortable. The speed of acquisition of the full protocol, and the relative short times for each individual sequence, is enabled by the acceleration capabilities of the newly installed Siemens Prisma 3T at the IHN. Data about the scanning session will be collected on an MRI data collection form (Appendix 20).

6. Neuropsychology testing and questionnaires

   To assess functional outcomes of immune and non-immune mediated disease, participants will undergo neuropsychology assessments. IPad assessments of intelligence skills will be conducted using age-appropriate tests:

   - Wechsler Intelligence Scale for Children 5th Edition (WISC-5) (6:0 to 16:11 years) (WISC-5; Wechsler, 2016)
   - Wechsler Preschool and Primary Scale of Intelligence 4th Edition (WPPSI-4) (2:6 to 7:7 years) (WPPSI-4; Wechsler, 2013)
   - The Wechsler Individual Achievement Test 2nd Edition (WIAT-3; Wechsler, 2005); subtests will include single word reading, pseudoword reading, reading comprehension and numeracy (4-15 years)
   - Adaptive Behavior Assessment System Second Edition (0-5yrs) (ABAS-III; Harrison & Oakland, 2003).

   Testing will be conducted by Assistant Psychologists under the supervision of a Paediatric Clinical Neuropsychologist employed by Birmingham Children's Hospital. This research assessment will take up to two hours to complete including breaks as needed by the participant. The assessments will be scored as per the standardised approach.

Study Setting

The research activities, i.e. consent, questionnaires, neuropsychology, OPM-MEG, MEG recording and MRI scanning will all take place with participants at the Aston University Institute for Health and Neurodevelopment (Aston IHN) in Birmingham, U.K. AIHN provides a world-class inter-disciplinary research environment, optimised for paediatric participants, and home to

cutting-edge imaging facilities including the OPM-MEG, MEG, a 3Tesla Siemens PRISMA MRI scanner, all underpinned by expert technical support, suites for clinical observation, and high-performance computing systems for data storage and analysis. AIHN is a CQC-registered facility. Aston IHN regularly takes referrals from Birmingham Children's Hospital as well as other epilepsy surgery centres from the UK and internationally to conduct clinical MEG scans for children awaiting surgery for refractory epilepsy.

Participant eligibility criteria

- Individuals (age range 2 yrs to 15 years 11 months) who have received a diagnosis of immune-mediated neurological disease e.g. autoimmune encephalitis[1], acute disseminated encephalomyelitis, multiple sclerosis. [2]
- Individuals who have received a diagnosis of a non-immune mediated neurological disease (age range 2 yrs to 15 years 11 months) e.g. stroke.

Additionally:

- Patients who can give informed consent/ assent and have a person with parental responsibility capable of giving informed consent on their behalf if aged <16 years.
- Male or female.

Exclusion criteria:

- There is metal in the body or any other contraindication that precludes MRI scanning at IHN, or child usually requires sedation for clinical MRI scans.
- Participant dissents.
- Individuals >16 years.

Participant Identification and Recruitment

Birmingham Children's Hospital (BCH) will be the primary research site. Professor Evangeline Wassmer and Professor Sukhvir Wright are both part of the clinical neurology department at the hospital and are responsible for the Neuroimmunology service. In addition, Great Ormond Street Hospital and Evelina Children's Hospital and Royal Manchester Children's Hospital will collaborate as research sites. All sites are part of the UK Childhood Neuroinflammatory Disease Network (UKCNID) and NHS England Paediatric Onset Multiple Sclerosis service. Identified families will be contacted by the clinician (via telephone, email, or face to face at clinic visit) and asked whether they wish to receive more information about the study. If interested they will be

asked for verbal consent by the clinician to allow their contact details (Name, Telephone Number and Email) as well as any contact preferences (e.g. preference of time of day, method of contact etc.) to be collected and shared with the research team. Verbal consent and contact details will be recorded on an electronic 'permission to contact' form (Appendix 1) by the clinician, and this will be emailed to the CI to be entered into a password protected database.

Consent:

To take part in this study, consent will be taken from the parent and/or guardian, and assent from the child themselves (if they are judged to have capacity) prior to the child and family participating in any aspect of the study.

Eligible participants will be identified at by appointed staff (local PI) working at the research sites. At this point, the participant and/or parents will be asked if their contact details (Name, telephone number, email) can be collected and passed onto the study team using a permission to contact form (Appendix 1). This will be emailed to the CI to be entered into a password protected database.

After families agree to being contacted, parents will be provided with hard copies of patient information sheets (Appendix 2,3,4) and/or a QR code to access digital copies (Appendix 18), and a copy of the consent forms.

Information sheets for young people will be given to children with images that demonstrate key concepts and explain procedures such as the OPM-MEG, MEG, MRI and neuropsychology assessments. These have been co-developed with young people and their carers. This is to ensure all children and young people taking part in the research are fully informed. Assent to take part in research will also be sought from all young people taking part in the study. Information Sheets and Assent/Consent forms for cases (children and parents) are provided in Appendices 2-17.

A member of the research team will contact families via the provided contact details (typically by phone/video call) to provide an overview of the study, explain the nature and objectives of the study and possible risks associated with their participation. This will be an opportunity for participants to ask any questions raised by the participant information sheets. If the family still wish to take part, an appointment will be made for the family to attend the IHN building on Aston University Campus (Appendix 29, 30).

At the time of the appointment a member of the research team at Aston University will tell families about the components of the study and explain the items on the consent forms in greater detail. Participants will then be invited again to take part in the study. If parents/guardians agree to take part, a member of the research team will seek and obtain written permission from the parent by completing the associated research consent form (Appendix 14).

Alongside consenting to take part in research and data processing/retention, parents/guardians will be asked to consent to several specific items as outlined in the consent form Appendix 14 and here:

1. Access to medical records - Consent will also be sought to access the medical records of the child or adolescent. The referring clinician will be asked to email CI Wright **through NHS email** the most recent clinical summary in the form of clinic letters and/or discharge summary. The clinical details will be extracted by the CI Wright on to the anonymised Study ID marked clinical report form (CRF, Appendix 21). This will reduce burden on the notifying clinician.

2. Incidental Findings requiring further clinical investigation – as described below.

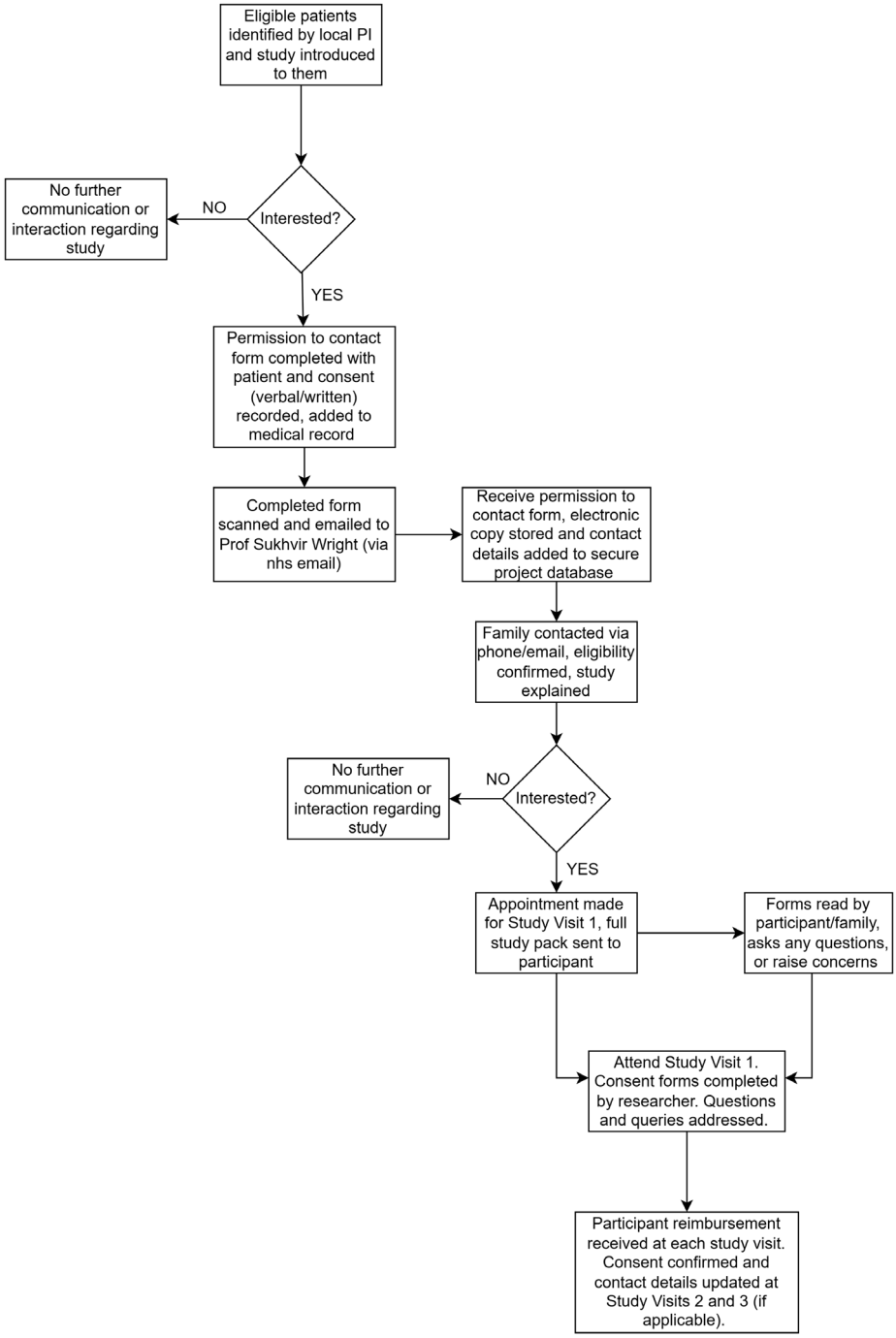
3. Sharing of research data with clinical teams - as described below.

For patients, notification of family and patient consent to participation in research, including a brief description of the procedures undertaken as a part of the research, will be sent to the clinical team (Appendix 31).

At each follow-up study visit at the IHN building on Aston University campus, families will be asked whether they have any more questions and will be asked to verbally consent to still taking part in the research study. This verbal consent will be documented by the researcher using the follow-up consent form (Appendix 15). If at any point during the follow-up period of the study, any parent/guardian/child dissents, they will cease participation in the study.

Consent/assent forms will contain participant identifiable information and so will be stored separately from deidentified research data, in a locked filing cabinet in the PI's office, with access limited to the PI or (under reasonable request) other members of the study team.

Consent procedure is summarised in the following flowchart:



Visual flowchart of consent procedure

Withdrawal from the study

Participants can withdraw from the study at any time without providing a reason. If this occurs, the participant's data will be deleted if requested. If the participant wishes to withdraw their data from the study after the OPM-MEG/MRI/MEG recordings have taken place, this will be possible until full data anonymisation which will take place 3 years after the end date of the study.

End of study

The study will end when 50 participants with immune-mediated and non-immune mediated neurological disease have completed the follow up visits and the cross-sectional data from 25 participants has been collected. In summary, the end of the study is defined as the final visit of the final participant.

Onsite Study Visit Procedures

1. Timing of initial and follow-up visits

   For the cross-sectional cohort there will only be one study visit (Study Visit 1). For the longitudinal cohort there will be three study visits (Study Visit 1,2,3) as outlined in Table 1. Arrangements for contacting participants to schedule Study visits 2 and 3 will be made at Study visit 1. At this point, the timing and nature of communication for this will be agreed with the family. For example, if they would prefer telephone or email contact. To encourage retainment, a study newsletter will be sent bi-annually with information and updates regarding the study along with an opportunity to update contact details if changed (Appendix 41).

2. OPM-MEG recording

   OPM-MEG recording will take place at IHN using the Mag4Health OPM-MEG. Recording procedures will follow all local procedures, rules and policies for research recordings. OPM-MEG scans will be performed by a fully-trained member of the research team. All participants will be provided with local documentation, including child-friendly and parent OPM-MEG information sheets (Appendices 5-7). To ensure compliance with the scan, and to improve tolerability, participants will be allowed to watch a video of their choosing whilst the recording occurs.

   Recordings will be pseudoanonymised, either using scanner vendor software or software provided independently, and transferred to the restricted access data storage / backup immediately after the scan has taken place. Access to these scans will be restricted to study staff and the lead research and clinical scientist Daisie Pakenham (for audit/review purposes). This data will then also be copied to the IHN high-performance computing cluster for processing, with electronic permissions used to restrict access to these files to only the research study team.

3. MEG recording

MEG recording will take place at IHN in the Wellcome Trust Laboratory for MEG Studies using the cryogenic MEGIN device. Recording procedures will follow all local procedures, rules and policies for research recordings. OPM-MEG scans will be performed by a fully-trained member of the research team. They will receive the local safety screening questionnaire (Appendix 19) to check for any contraindications to scanning. All participants will be provided with local documentation, including child-friendly and parent MEG information sheets (Appendices 11-13). To ensure compliance with the scan, and to improve tolerability, participants will be allowed to watch a video of their choosing whilst the recording occurs.

Recordings will be pseudoanonymised, either using scanner vendor software or software provided independently, and transferred to the restricted access data storage / backup immediately after the scan has taken place. Access to these scans will be restricted to study staff and the lead research and clinical scientist Sian Worthen (for audit/review purposes). This data will then also be copied to the IHN high-performance computing cluster for processing, with electronic permissions used to restrict access to these files to only the research study team.

4. <u>MRI scan</u>

MRI scanning will take place at IHN using the Siemens 3T Prisma MRI scanner. Scanning procedures will follow all local procedures, rules and policies for research scanning. All participants will be provided with local documentation, including parent (Appendix 8) and child-friendly MRI information sheets (Appendix 9,10). They will receive the local safety screening questionnaire (Appendix 19) to check for any contraindications to scanning (such as aneurysm clips in brain, metal dental implants, metallic fragments in eye or anywhere else, insulin pump, metal implants, hearing aid or a prosthetic device containing metal). MRI scans will be attended by a fully-trained member of the research team, and a suitably qualified member of staff (typically a state-registered radiographer) who will conduct the scan, in line with local policy. Before undergoing the MRI, a trained MRI technician (typically a radiographer) will run through this safety screening questionnaire to ensure safety during scanning. Safety screening will be repeated for each scanning session, and for all individuals who will enter the scanning room (parents/guardians will be able to enter the scanning room to support child participants if needed, however they will still need to go through the same screening procedures as the child participant). Safety screening questionnaires will contain participant identifiable information and so will be stored separately from deidentified research data,

in a locked filing cabinet in the PI's office, with access limited to the PI or (under reasonable request) other members of the study team.

Sedation or general anaesthesia will not be used, and the investigation will only be possible if the participant can undergo the investigation without sedation or anaesthesia. This ensures there is no additional risk to the participants. To ensure compliance with the scan, and to improve tolerability, participants will be given ear protection in the form of headphones and will be allowed to watch a video of their choosing whilst the scan occurs. Scans will be pseudoanonymised, either using scanner vendor software or software provided independently, and transferred to the restricted access data storage / backup immediately after the scan has taken place. Access to these scans will be restricted to study staff and the lead research radiographer (for audit/review purposes). This data will then also be copied to the IHN high-performance computing cluster for processing, with electronic permissions used to restrict access to these files to only the research study team.

5. Neuropsychology

   Standardised neuropsychology assessments will be completed with participants conducted by Assistant Psychologist supervised by Consultant Clinical Psychologist, Dr Jo Horton. These will be completed on an iPad as is standard at Birmingham Children's Hospital. Participants will be given as many breaks as necessary to ensure that they are able to give their best attempt on the day, so that their attempt best reflects their actual abilities. These will be scored as per the standardised approach. Test scores will be entered in a password-protected database (.csv file) at the earliest convenience by a member of the research team, with access restricted to only the research team. In all instances, general feedback based on qualitative descriptions of scores, identifying potential strengths and weaknesses, will be sent to the family. This is our standard practice to date in our research, and in keeping with accepted practice (Appendices 32-34).

6. Questionnaires

   Questionnaires will be completed by parents/guardians onsite, on paper-based forms (Appendices 22-28). Typically, this would be done whilst the participant was being scanned. Researchers will give explanations of how to fill out the questionnaires and will be available to answer any questions/queries/concerns raised. They will be informed not to put their or their child's name on the forms. These paper-based forms will be collected before the family leaves. If a family needs extra time to complete the questionnaire, a

space onsite will be found to allow them to do so. In the unlikely scenario that a parent/guardian cannot complete the questionnaires at the research visit, a stamped addressed envelope can be provided for them to return the forms in the post. Paper-based forms will be identifiable with the participants study ID and will be stored with the participants research folder in a locked office, with access restricted to the study team. Data will be entered in a password-protected database (.csv file) at the earliest convenience by a member of the research team, with access restricted to only the research team.

7. Reimbursement for study visits

   It is appropriate to reimburse families for the burden and inconvenience caused by participating in this study. They will be offered financial reimbursement to cover travel (mileage or standard rail travel) to and from Aston, and accommodation overnight if coming from outside the West Midlands (e.g., Manchester and London participants). Participants will also be given online Amazon vouchers emailed to parent/guardian. They will receive £25 for first study visit, and £40 for each return visit. An acknowledgement of reimbursement will be provided (Appendix 35).

Risks and burdens:

1. Participant Safety

- Research activity on the study is governed by the requirements of the sponsor and the AIHN. Participant safety has been assessed in research risk-assessments conducted by senior facility leads covering activities such as OPM-MEG, MEG and MRI. These risk assessments are in Appendices 38-40.

2. MRI

- The research MRI scans performed in this study for are not clinical investigations, they have been selected to answer specific research hypotheses, rather than to answer specific clinical/diagnostic queries at the level of individual patients. The MRI investigations undertaken during this study may potentially highlight findings that need to be investigated as incidental findings. Incidental findings are “a finding that has potential health or reproductive importance, unknown to the participant, which is discovered in the course of conducting research, but is unrelated to the purpose and beyond the aims of the study" (Royal College of

Radiologists & Wellcome, 2012). In the case of a clinical population such as this who are already undergoing MRI investigation clinically, an incidental finding would be something that it unexpected given the context of the diagnoses under study. For instance, if an MRI revealed white matter lesion in patient with multiple sclerosis, this would not be an incidental finding as this is typical of the presentation, however a cerebral aneurysm – not typical, would be reported as an incidental finding to be followed up via the IHN incidental finding policy. Briefly, this involves review of anonymised images by a clinically-trained individual to assess clinical significance and, if considered to be needing follow-up, participant's GP will be contacted. Further details about incidental findings found during MRI can be found in the MRI information sheet (Appendix 8). Consent will be sought to ensure that families are aware of these risks and to give us permission to share information and details where necessary. If families DO NOT consent to these items, they will not be able to take part in the study.

- Requirement for additional images and scans for the purpose of research may invoke further stress on families. The study design reduces additional burden by keeping scan sequences short and ensuring only one day maximum required for each study visit. At any point during the initial discussion of the scan or when they enter the scanning environment should a child exhibit signs of dissent or distress, we will stop the session. IHN has trained staff with paediatric experience to support children.

3. Neuropsychology assessments

- The neuropsychological assessments performed in this study are not clinical investigations, they have been selected to answer specific research hypotheses, rather than to answer specific clinical/diagnostic queries at the level of individual patients. Assessment of participants may reveal that their performance is below age-expectations as they are being performed within 9 months of disease onset during recovery phase.
- Standard practice in our research to date is that all parents/guardians receive a written report outlining their child's results (Cover letter Appendix 32, 33 Report template Appendix 34).
- Consent will be sought to ensure that families are aware of these risks and to give us permission to share information and details where necessary, for example, if

the clinical team request copies of scores. If families DO NOT consent to these items, they will not be able to take part in the study.

4. OPM-MEG/MEG

- OPM-MEG is a very safe technique and completely non-invasive that solely detects naturally occurring brain signals; it does not emit, apply or alter anything.
- There is a risk of mild discomfort during the OPM-MEG recording, specifically the slight weight of the MEG helmet and its wires. The weight of the wires is greatly reduced by suspending them from above the patient's head and them being supported by a bespoke gantry. Participants can ask to stop the recording at any time, and someone will be there to help the remove the helmet.
- The MEG may be uncomfortable as the child will be asked to remain very still.
- The OPM-MEG and MEG system are housed in magnetically shielded rooms, to which the door will be closed during recording. The room is large yet there is a risk for people who suffer from claustrophobia. However, claustrophobia will be screened for in the patient questionnaire to prevent any risk of this. The participants will also be shown the room before going in and will be able to withdraw at any time. The child will always have the parent in the room with them and will be monitored at all times by the research team and will be free to leave the room whenever they please.

Adverse events

Any adverse events associated with the specific procedures listed above will be reported immediately to the chief investigator who will formally report them to the Aston University Research Integrity Office, NHS REC and relevant Trust R&D office.

Statistics and data analysis

Analysis and Power: FOR OPM-MEG (main study measure) we will use graph theoretical analysis of resting-state brain networks and measure network efficiency (global and local) and modularity. A priori power analyses (in G*Power) shows that assuming a strong two-tailed individual t effect size (f^2 = .35) is observed for the effect of the graph measure (which is what is required from a relevant biomarker) 25 participants are need to reach a sufficiently high power (1-β = .80). This is the sample size aimed for in recruitment. In our preliminary study, samples sizes of 12 yielded group level differences.[5]

Data management plan

Consent to Data Sharing:

Consent will be sought for sharing of participant data through open access data sets and access to participant clinical/medical data.

Open access:

Data from this cohort may be highly valuable to future research efforts. Thus, we will ask participants to provide written informed consent to make their anonymised data freely available for reanalysis by the team in future studies, and to researchers outside of the study team for use in ethically approved projects. Consent form for open access data sharing is in in the Appendices (Appendix 44). Specifically, neuroimaging (MRI), questionnaire, neuropsychology (summary scores) and demographic data that are suitable for sharing will be made available, using open-access data repositories platforms such as OSF (osf.org) or other suitable platforms which meet current best practice within the field, in relation to local and national regulations (i.e. GDPR). Open-access sharing of data will open happen once the linking document (linking study ID to personal identifiable data i.e. name) is destroyed (3 years after study end), to ensure that shared data is truly anonymous, not pseudo-anonymised. Once data are made available for sharing the study team will no longer have exclusive use of the data.

MRI scans will be shared in a minimally processed format, however MRI scans with identifiable facial information will be 'de-faced', as is typical for the neuroimaging field and identifiable metadata will be removed from the files. All data pertaining to an individual will be linked through a participant code that does not identify the individual. It will be explicit in the information provided and consent that personally identifying information will not be shared (i.e. DOB).

At all times current best practice within the field, in relation to local and national regulations (i.e. GDPR) will be followed and Aston University's Research Integrity Office will be consulted. All information sheets and consent forms for participants reflect these decisions.

Data will only be shared from those participants who consent explicitly to this in the consent form and consent for data sharing in this way is not a requirement for taking part in the study.

Data sharing with clinical teams:

If requested by the family and/or participant, or the clinical team (neurology or psychology) we will gain consent to share the relevant data (neuropsychology scores) (Appendix 33).

Participant data:

The Chief Investigator will act as custodian of the study data. The following guidelines will be strictly adhered to:

• Participant data will be pseudo-anonymized at all times and will be fully anonymized three years after the end of the study.

•All study data will be stored in accordance with University data storage policies for research data.

•Study data will be archived in accordance with Aston University Archive Policies and Procedures for archiving of clinical research data.

Personal Data (Consent form, safety screening questionnaire)

Details will be entered into a password protected database (.csv file). The password protected database will be stored on the cloud storage platform recommended by university data storage policies (BOX). If emailed, the clinician paper-copy of the file is to be securely destroyed asap once shared with the research team. Consent/assent/MRI safety screening questionnaire/permission-to-contact forms will contain participant identifiable information and so will be stored separately from deidentified research data, in a locked filing cabinet in the PI's office and, as soon as is possible, these will be scanned to be digitized, and the original copies destroyed securely (i.e. shredded). Digital copies will be stored on the cloud storage platform recommended by university data storage policies (BOX), with access limited to the PI or (under reasonable request) other members of the study team.

Clinical Report Form Data

The CI will complete the clinical report form proforma digitally with information provided by the notifying clinician through secure NHS email. This form will be anonymized to only contain a study ID code and will be stored with the participants research folder in a locked office, with access restricted to the study team. Data will be entered in a password-protected database (.csv file) at the earliest convenience by a member of the research team, with access restricted to only the research team. The password protected database will be stored on the cloud storage platform recommended by university data storage policies (BOX).

MRI Data

Scanner hardware requires participants to be registered with identifiable data (name/DOB/height/weight). Once data transfer is successful the record will be deleted. This record will not contain ID code. Once scanned, MRI Data will be pseudo anonymised, either using

scanner vendor software or software provided independently, and transferred to the restricted access data storage / backup immediately after the scan has taken place. The PACS database system at Aston allows scans to be directly transferred from the scanner, which removes the need for memory sticks and manual transfer. All data goes to a backup database in the PACS and also into a project specific network folder which only the research team will have access to. Access to these scans will be restricted to study staff and the lead research radiographer (for audit/review purposes). This data will then also be transferred to the IHN high-performance computing cluster for processing, with electronic permissions used to restrict access to these files to only the research study team. The resulting analysis files will be regularly backed up.

Questionnaire, Neuropsychology, and demographic data

Data will be entered in a password-protected database (.csv file) at the earliest convenience by a member of the research team, with access restricted to only the research team. The password protected database will be stored on the cloud storage platform recommended by university data storage policies (BOX). Digital data will be stored on the cloud storage platform recommended by university data storage policies (BOX). Neuropsychology test data will be shared with the named clinician referring the participant if the participant consents/assents to this.

Data Storage

Aston University will maintain an archive of the study data on a secure, password-protected computer system. All clinical data for each patient will be organised together in a folder system, identified by participant ID, on a secure server which is regularly backed up and archived according to best practice. Aston IHN will keep a record of each set of participant IDs so that records can be linked with consent forms if required.

Data retention

Personal Data - Personal data stored within the linking document (Names) and permission to contact form database will be retained for 3 years after the study end. Consent will be sought to keep personal details so updates on their clinical condition can be sought from the clinical care team for up to 3 years after they have taken part in the study. However, participants have the right to withdraw at any time during the study and no further data will then be collected. Three years after the end of the study the personal data within the linking document will be destroyed and securely deleted from BOX. Once this linking document is destroyed, research data will be fully anonymized. This storage of personal data will also allow us to contact participants who indicate a willingness to be contacted for PPIE/future studies. Summary findings of the research can also be communicated to those who have consented to this.

In line with Aston University's Research Data Management Policy, remaining documents containing personal data (consent forms) will be archived locally and retained for a period of six years after study end, alongside hard copies of approved consent forms, information sheets, & records relating to ethical approval for instance. During this time, this document will be stored on BOX as per the Aston University's Research Data Management Policy, with access limited to the PI – these will be password protected. This will then be securely deleted from BOX after 10 years.

Research Data: Open Access Sharing - In line with Aston University's Research Data Management Policy, research data will be archived locally and retained for 6 years after study end. After the 3-year retention period of the linking document, this data will become fully anonymised.

Data from this cohort may be highly valuable to future research efforts. Thus, we will ask participants to provide written informed consent to make their anonymised data freely available for reanalysis by the team in future studies, and to researchers outside of the study team (upon request). Specifically, neuroimaging (MRI, MEG and OPM-MEG), questionnaire, neuropsychology (summary scores) and demographic data that are suitable for sharing will be made available, using open-access data repositories platforms such as OSF (osf.org) or other suitable platforms which meet current best practice within the filed, in relation to local and national regulations (i.e. GDPR). Open-access sharing of data will open happen once the linking document (linking study ID to personal identifiable data i.e. name) is destroyed, to ensure that shared data is truly anonymous, not pseudo-anonymised.

The linking document (linking study ID to name) will be retained for 3 years (in case of need to identify a specific participant's research data) before being destroyed by the PI, to fully anonymise the data. A local copy of the dataset will still be retained for the 6-year period, even after open-access sharing and fully anonymising the data, to ensure that the 'original' dataset is available for validation of the open/shared dataset. Data will only be openly shared from those participants who consent explicitly to this in the consent form and consent for data sharing in this way is not a requirement for taking part in the study. It is the responsibility of the PI to ensure the appropriate sharing of the research data as outlined here.

MONITORING, AUDIT & INSPECTION

This study will be monitored by the CI Sukhvir Wright. Monitoring will involve regular checks of the recruitment rate, study completion rate, and meetings with the research team to identify

practical problems. Regular steering group meetings will also monitor governance and ensure study is on track and meeting needs of participants. The research will be monitored and audited by the Sponsor.

ETHICAL AND REGULATORY CONSIDERATIONS

Research Ethics Committee (REC) review & reports

- before the start of the study, approval will be sought from NHS REC and HRA and HRCW REC for the trial protocol, informed consent forms and other relevant documents.
- substantial amendments that require review by REC will not be implemented until the REC grants a favourable opinion for the trial and/or NHS R&D departments before they can be implemented in practice at sites)
- all correspondence with the REC will be retained in the Investigator Site File
- the Chief Investigator will notify the REC of the end of the study
- if the study is ended prematurely, the Chief Investigator will notify the REC, including the reasons for the premature termination
- within one year after the end of the study, the Chief Investigator will submit a final report with the results, including any publications/abstracts, to the REC

Peer review

This study has received peer review internally within Aston University and external peer review when submitted for Wellcome Career Development Award (Appendix 42).

Public and Patient Involvement

The development of this proposal has integrated feedback of what concerns our patients and their families most about their child. The top concerns from parents were: social skills (e.g. “X does not have established friendships due to his lack of skills/awareness”), academic performance (“X struggles reading some words and concentration is a struggle”), attention (“X gets unusually distracted and finds it hard to write”), their child’s future and independence (“Lacks insight into his needs”). This has fed into the design of the proposal. I have had active representation/participation from The SHAPE network (Epilepsy Research Institute PPI group)

and Encephalitis Society from before study commencement, and this will continue throughout the study alongside representation on the steering group. The patient/parent representative we have a longstanding relationship with having treated their child from 2-18yrs, and from their previous participation in our preliminary MEG study. Their feedback and ongoing involvement will be invaluable in this project. The information sheets and study summary have been reviewed and co-developed with our IHN youth advisory group, healthy controls, and patient representatives from Encephalitis International and the SHAPE network (example feedback Appendix 43).

Protocol compliance

Deviations from the protocol will be reported to the sponsor in 24 hours.

Financial and other competing interests for the chief investigator, PIs at each site and committee members for the overall study management

There are no competing or financial interests.

Indemnity

Insurance and/or indemnity to meet the potential legal liability of the sponsor for harm to participants arising from the **management** of the research will be covered by Aston University insurance.

Insurance and/or indemnity to meet the potential legal liability of the sponsor or employer for harm to participants arising from the **design** of the research will be covered by Aston University insurance.

Insurance and/or indemnity to meet the potential legal liability of investigators/collaborators arising from harm to participants in the **conduct** of the research will be covered by the NHS indemnity scheme or professional indemnity for participants recruited at NHS sites only, and Aston University insurance will apply for research sites that are not covered by the NHS indemnity scheme.

No equipment will be provided to NHS sites for the purposes of this study.

Amendments

The responsibility for making amendments resides with the Chief Investigator and submitted via the Sponsor and this includes notification of all parties including the NHS REC, HRA and all sites.

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Appendices

Appendix No.	Title/Description	Filename
1	Permission to contact form	Appendix1_OMEGAMIND_Permissiontocontact_v1_22_10_25
2	Participant Information Sheet (PIS) parent/guardian	Appendix2_OMEGAMIND_PIS_Parent_Guardian_v1_22_10_25
3	Participant Information Sheet (PIS) age 6-9 years	Appendix3_OMEGAMIND_PIS_Child_6-9yrs_v1_18_11_25
4	Participant Information Sheet (PIS) age 10-15 years	Appendix4_OMEGAMIND_PIS_Child_10_15_yrs_v1_18_11_25
5	Aston IHN Participant Information Sheet (PIS) parent/guardian OPM-MEG	Appendix_5_IHN_OPM-MEG_InfoSheet_Adult_&_Over16s_Version1
6	Aston IHN Participant Information Sheet (PIS) age 6-9 years OPM-MEG	Appendix_5_IHN_OPM-MEG_InfoSheet_6_9_Version1
7	Aston IHN Participant Information Sheet (PIS) age 10-15 years OPM-MEG	Appendix_5_IHN_OPM-MEG_InfoSheet_10-15_Version1
8	Aston IHN Participant Information Sheet (PIS) parent/guardian MRI	Appendix_8_IHN_MRI_InfoSheet_Version2
9	Aston IHN Participant Information Sheet (PIS) age 6-9 years MRI	Appendix_9_IHN_MRI_InfoSheet_6-9_Version3
10	Aston IHN Participant Information Sheet (PIS) age 10-15 years MRI	Appendix_10_IHN_MRI_InfoSheet_10-15_Version2
11	Aston IHN Participant Information Sheet (PIS) parent/guardian MEG	Appendix_11_IHN_MEG_InfoSheet_Version2
12	Aston IHN Participant Information Sheet (PIS) age 6-9 years MEG	Appendix_12_IHN_MEG_InfoSheet_6-9_Version2
13	Aston IHN Participant Information Sheet (PIS) age 10-15 years MEG	Appendix_13_IHN_MEG_InfoSheet_10-15_Version2
14	Consent/Assent: Consent form for Parents/Guardians	Appendix 14 _OMEGAMIND_CONSENT_FORM_v1_221025
15	Consent/Assent: Follow-up Consent form for Parents/Guardians	Appendix15_OMEGAMIND_FollowupConsent_v1_22_10_25
16	Consent/Assent: Assent form for Young People (6-9)	Appendix16_OMEGAMIND_AssentForm_6-9_v1_22_10_25
17	Consent/Assent: Assent form for Young People (10-15)	Appendix17_OMEGAMIND_AssentForm_10-15_v1_22_10_25
18	Study info card with QR code	Appendix 18_OMEGAMIND_Study Info Card_V1_18_11_2025
19	Aston IHN MRI Safety Screening Questionnaire	Appendix_19_IHN_MRIMEG_SafetyScreeningForm_Version2
20	MRI: MRI Data Collection Form	Appendix20_OMEGAMIND_MRICollectionForm_v1_22-10_25
21	Clinical Report Form	Appendix21_OMEGAMIND_CRF_v1_22_10_25
22	Questionnaires: Demographic Questionnaire	Appendix22_OMEGAMIND_Demographics_v1_22-10_25

23	Questionnaires: SDQ	Appendix23_OMEGAMIND_SDQ_v1_22-10_2025
24	Questionnaires: Ped QoL	Appendix24_OMEGAMIND_ PedQoL_v1_22-10_25
25	Questionnaires: PedQoL Multidimensional Fatigue	Appendix25_OMEGAMIND_ PedQoL_Fatigue_v1_22-10_25
26	Questionnaires: SDSC	Appendix26_OMEGAMIND_ SDSC_v1_09052024
27	Questionnaires: CBCL	Appendix27_OMEGAMIND_ CBCL_v1_22-10_25
28	Questionnaires: BRIEF	Appendix28_OMEGAMIND_ BRIEF_v1_28102025
29	Letter: Appointment Letter	Appendix29_OMEGAMIND_AppointmentLetter_v1_23_10_25
30	Letter: Map to get to IHN	Appendix30_OMEGAMIND_ AppointmentMap_v1_23_10_25
31	Letter: Participation Letter for clinical team	Appendix31_OMEGAMIND_Participationletter_v1_231025
32	Letter: Neuropsychology Report Parent Cover Letter	Appendix32_OMEGAMIND_NeuropsychParentCoverLetter_v1_18_11_2025
33	Letter: Neuropsychology Report Clinician Cover Letter	Appendix33_OMEGAMIND_NeuropsychClinicianCoverLetter_v1_18_11_2025
34	Letter: Neuropsychology Report template	Appendix34_OMEGAMIND_NeuropsychReportTemplate_v1_10112025
35	Schedule/Acknowledgement of Reimbursement	Appendix35_OMEGAMIND_ReimbursementForm_v1_231025
36	Delegation of Duties Log: Aston University	Appendix36_OMEGAMIND_ DoD-Aston_ v1_231025
37	Delegation of Duties Log: PIC site	Appendix37_OMEGAMIND_DoD_Research_site_ v1_231025
38	Aston IHN Risk Assessment OPM-MEG	Appendix_38_IHN-RA-OPM-MEG_Generic_V1
39	Aston IHN Risk Assessment MRI	Appendix_39_IHN-RA-MRI_Generic_V3
40	Aston IHN Risk Assessment MEG	Appendix_40_IHN-RA-MEG_Generic_V3
41	Newsletter template	Appendix41_newsletter template_OMEGAMIND_v1_231025
42	Expert reviews Wellcome	Appendix_42_ExpertReviewSummary
43	PIS feedback and changes	Appendix43_PISfeedback_example
44	Open access consent	Appendix44_O-MEGA_MIND_OpenAccessConsent_v1_151225