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A study of brain activity in visual snow syndrome and migraine

Submission date	Recruitment status	[X] Prospectively registered
10/06/2026	Not yet recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
13/07/2026	Ongoing	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
13/07/2026	Nervous System Diseases	[X] Record updated in last year

Plain English summary of protocol

Background and study aims

Visual snow syndrome (VSS) is a neurological condition causing constant flickering dots across the entire visual field, often alongside other visual disturbances such as light sensitivity and afterimages. Many people with VSS also have migraines. There are currently no proven treatments. Brain imaging suggests VSS may involve overactivity in visual brain areas, linked to an imbalance between the excitatory brain chemical glutamate and the inhibitory chemical GABA. This study uses ultra-high-field (7 Tesla) MRI to measure these chemicals directly in people with VSS and migraine and tests whether lamotrigine (a medication that reduces glutamate release) can alter brain chemistry and improve symptoms.

Who can participate?

Adults aged 18 years and over with a diagnosis of VSS (with or without migraine), migraine without VSS, and healthy volunteers

What does the study involve?

Participation lasts up to 8 weeks (1–2 weeks for healthy volunteers). All participants attend a telephone pre-screening and a baseline 7-Tesla MRI scan at St Thomas' Hospital, London, and complete symptom questionnaires. Participants with VSS or migraine are then randomly assigned to lamotrigine or placebo for 5 weeks, keep an electronic symptom diary, return for a second scan, taper off medication over 2 weeks, and have a final telephone follow-up. Healthy volunteers complete the study after the first scan.

What are the possible benefits and risks of participating?

There is no direct medical benefit, though findings may help develop future treatments. Participants receive £50 per visit plus travel reimbursement up to £100. Risks include temporary dizziness from high-field MRI and potential lamotrigine side effects (headache, nausea, rash). Participants with known risk factors for serious reactions are excluded and all are monitored throughout.

Where is the study run from?

Participants are identified through King's College Hospital (UK). Scan visits take place at the Advanced Neuroimaging Facility, St Thomas' Hospital (UK).

When is the study starting and how long is it expected to run for?
September 2026 to August 2029

Who is funding the study?
Medical Research Council (MRC) Clinician Scientist Fellowship (UK)

Who is the main contact?
Dr Francesca Puledda, vs-research@kcl.ac.uk

Contact information

Type(s)
Public, Scientific, Principal investigator

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Integrated Research Application System (IRAS)
362088

Central Portfolio Management System (CPMS)
74550

Grant Code
APP60807

Study information

Scientific Title
Functional and metabolic characterisation using 7T neuroimaging in visual snow syndrome and migraine (FOCUS-VSM)

Acronym
FOCUS-VSM v1.0

Study objectives

Primary Objective:
1. To use proton spectroscopy (^{1}H-MRS) at ultra-high-field (7-Tesla, 7T) to study brain metabolism and function in patients with visual snow syndrome (VSS) and migraine (MO), compared to healthy volunteers (HV), both at rest and following a visual stimulus (^{1}H-fMRS)

Secondary Objective:
1. To determine the effect of oral lamotrigine (LTG) on brain glutamate metabolism measured via ^{1}H-MRS in patients with VSS and migraine

Exploratory Objectives:
1. To determine differences between visual cortex metabolism in patients with VSS compared to patients with migraine
2. To investigate changes in functional connectivity using resting-state fMRI in patients with VSS and migraine, before and after oral LTG
3. To investigate the changes in VSS symptoms following oral LTG administration

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 13/07/2026, London – Dulwich Research Ethics Committee (Health Research Authority 2nd Floor 2 Redman Place Stratford, London, E20 1JO, United Kingdom; +44 (0)207 104 8169; dulwich.rec@hra.nhs.uk), ref: 26/LO/0464

Primary study design
Interventional

Study design
Randomized controlled trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Visual snow syndrome

Interventions
The study design consists of a randomized, double-blind design with two treatment conditions (oral placebo or oral lamotrigine) and neuroimaging with magnetic resonance imaging /spectroscopy. The design involves a screening telephone visit, two in-person visits to the Advanced Neuroimaging Facility at St Thomas' Hospital and one telephone follow-up visit. The study will involve three participant groups: VSS participants, migraine participants, and healthy controls.

Neuroimaging protocol:
V1 and V2 will involve MRI scanning at 7T. These visits will take place at the 7 Tesla Siemens Terra System MRI at St Thomas' Hospital and involve a 70-90-minute scanning session (depending on participant compliance) with the option of a 15-30-minute break.

Pharmacological intervention protocol:
Each subject will participate in two treatment arms in which they will receive either oral LTG or

oral placebo gradually up-titrated over the course of 4 weeks and maintained at a stable dose in week 5. They will then return for a second scanning visit, after which the medication will be down-titrated to a stop in 14 days following Visit 2.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Lamotrigine

Primary outcome(s)
1. Visual cortex glutamate and GABA concentrations measured using proton magnetic resonance spectroscopy at 7 Tesla (7T ^{1}H-MRS), acquired at rest and during visual stimulation (functional 1H-MRS), at baseline (Visit 1) and at 5 weeks post-randomisation (Visit 2)

Key secondary outcome(s)
1. Change in visual cortex glutamate concentration in response to lamotrigine versus placebo is measured using 7T ^{1}H-MRS at Visit 1 and Visit 2 (5 weeks)
2. Differences in visual cortex glutamate and GABA concentrations between participants with visual snow syndrome and participants with migraine are measured using 7T ^{1}H-MRS at Visit 1 and Visit 2 (5 weeks)
3. Resting-state functional connectivity is measured using blood oxygenation level-dependent functional MRI at 7 Tesla (7T BOLD fMRI) at Visit 1 and Visit 2 (5 weeks)
4. Visual snow syndrome symptom severity is measured using the Visual Snow Scale and Diary at Visit 1 and Visit 2 (5 weeks), and at 7-week telephone follow-up
5. Visual sensitivity is measured using the Visual Sensitivity Questionnaire (VSQ) at pre-screening, baseline (Visit 1), at 5 weeks post-randomisation (Visit 2), and at 7 weeks (telephone follow-up)
6. Headache impact is measured using the Headache Impact Test (HIT-6) at pre-screening, baseline (Visit 1), at 5 weeks post-randomisation (Visit 2), and at 7 weeks (telephone follow-up)
7. Migraine-related disability is measured using the Migraine Disability Assessment Test (MIDAS) at pre-screening, baseline (Visit 1), at 5 weeks post-randomisation (Visit 2), and at 7 weeks (telephone follow-up)
8. Depressive symptoms are measured using the Patient Health Questionnaire (PHQ-8) at pre-screening, baseline (Visit 1), at 5 weeks post-randomisation (Visit 2), and at 7 weeks (telephone follow-up)
9. Anxiety symptoms are measured using the Generalised Anxiety Disorder questionnaire (GAD-7) at pre-screening, baseline (Visit 1), at 5 weeks post-randomisation (Visit 2), and at 7 weeks (telephone follow-up)
10. Health-related quality of life is measured using the EuroQol five-dimension five-level questionnaire (EQ-5D-5L) at pre-screening, baseline (Visit 1), at 5 weeks post-randomisation (Visit 2), and at 7 weeks (telephone follow-up)
11. Migraine and visual snow syndrome symptom frequency and severity are measured using electronic headache and visual snow diaries continuously from Visit 1 to 7-week telephone follow-up

Completion date
31/08/2029

Eligibility

Key inclusion criteria
Group 1: VSS patients
1. Diagnosis of visual snow syndrome following the published criteria
2. Aged >18 years
3. Able to provide written informed consent in English
4. Evidence of a personally signed and dated informed consent document indicating that the subject (or a legally acceptable representative) has been informed of all pertinent aspects of the trial detailed in the patient information sheet, informed consent form, and in the protocol
5. Willing and able to comply with scheduled visits, lifestyle guidelines and trial procedures, including using a reliable method of birth control whilst on the medication for female participants
6. No history of worsening of VSS with prior medications

Group 2: Migraine patients
1. Diagnosis of migraine with or without aura following the International Classification of Headache Disorders (ICHD-3) beta criteria
2. Aged >18 years
3. Able to provide written informed consent in English
4. Evidence of a personally signed and dated informed consent document indicating that the subject (or a legally acceptable representative) has been informed of all pertinent aspects of the trial detailed in the patient information sheet, informed consent form, and in the protocol
5. Willing and able to comply with scheduled visits, lifestyle guidelines and trial procedures, including using a reliable method of birth control whilst on the medication for female participants
6. No concomitant diagnosis of VSS

Group 2: Healthy controls
1. Aged >18 years
2. Able to provide written informed consent in English
3. Evidence of a personally signed and dated informed consent document indicating that the subject (or a legally acceptable representative) has been informed of all pertinent aspects of the trial detailed in the patient information sheet, informed consent form, and in the protocol
4. Willing and able to comply with scheduled visits, lifestyle guidelines (see below) and trial procedures
5. No concomitant diagnosis of VSS or migraine

Healthy volunteers allowed
Yes

Age group
Mixed

Lower age limit
18 Years

Upper age limit
100 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Pregnancy and breastfeeding
2. Any metal implants in the head or body (except for titanium and dental work)
3. Any other medical and safety contraindications to undergo ultra-high-field MRI (e.g., large tattoos, ongoing dizziness and vertigo)
4. History of epilepsy or of prior lamotrigine use (for VSS and MO groups only)
5. History of adverse or allergic reactions to drugs (for VSS and MO groups only)
6. Family history of Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN) (for VSS and MO groups only)
7. Known or suspected carriers of HLA alleles associated with SJS or TEN (e.g., HLA-B15:02, HLA-A24:02, and HLA-B38:01) (for VSS and MO groups only)
8. Regular smoking of >6 cigarettes a day
9. Regular intake of medications acting on the central nervous system
10. Regular use of recreational drugs
11. History of psychosis or psychological disease either (a) requiring ongoing psychoactive drugs, or (b) that the investigator has reason to believe will either affect the patient’s neural pathways or hinder the performance of the patient regarding the ability to successfully complete the tasks required of them according to the protocol
12. Any person unable to understand written or spoken English
13. Subjects unwilling to comply with lifestyle guidelines necessary for the study
14. Subjects who are or have recently (last 30 days) been involved in any interventional clinical trial
15. Any other condition that in the opinion of the investigator would make the subject unsuitable for the study

Date of first enrolment
01/09/2026

Date of final enrolment
31/05/2028

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Guy's and St Thomas' NHS Foundation Trust
St Thomas' Hospital
Westminster Bridge Road
London

England
SE1 7EH

Sponsor information

Organisation
King's College London

ROR
https://ror.org/0220mzb33

Funder(s)

Funder type
Government

Funder Name
Medical Research Council

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, Medical Research Committee and Advisory Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon request from Dr Francesca Puledda (francesca.puledda@kcl.ac.uk). Anonymised clinical, questionnaire, and neuroimaging data (CSV files, DICOM and NIFTI format) will be made available to researchers at the time of publication and retained for a minimum of 10 years from the end of the grant period. Access is subject to a data access agreement prepared in accordance with MRC data-sharing guidelines, and data will be available for analyses consistent with the original study aims. Participant consent for anonymised data sharing will be obtained at

enrolment. All data will be fully anonymised and defaced prior to sharing to remove personal identifiers. There are no anticipated ethical or legal restrictions beyond those managed through the data access agreement process.

IPD sharing plan summary

Available on request