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Testing gabapentin to treat distorted senses of smell after a viral infection

Submission date 16/09/2025	**Recruitment status** Recruiting	[_] Prospectively registered [X] Protocol
Registration date 10/11/2025	**Overall study status** Ongoing	[_] Statistical analysis plan [_] Results
Last Edited 27/07/2026	**Condition category** Ear, Nose and Throat	[_] Individual participant data [X] Record updated in last year

Plain English summary of protocol

Background and study aims

Parosmia is a condition where the sense of smell becomes distorted. People with parosmia often report that normal smells, such as coffee or food, are unpleasant or foul. This condition is commonly seen after viral infections, especially COVID-19. It can have a serious impact on daily life.

At the moment, there are no proven treatments. This study will investigate whether a medicine called gabapentin can help reduce the symptoms of parosmia. Gabapentin is already used to treat nerve pain and epilepsy. It works by calming overactive nerves and may help reduce the abnormal smell signals that cause parosmia.

The main question the research aims to answer is whether gabapentin is a safe and effective treatment for people with parosmia after a viral infection. If successful, this treatment could offer new hope to many people affected by this condition.

Who can participate?

To take part, people must be aged 18 to 65 and have had parosmia for more than 3 months but less than 3 years after a viral illness.

What does the study involve?

The study is a clinical trial. People who take part will be randomly placed into one of two groups. One group will receive gabapentin and the other will receive a placebo. A placebo is a capsule that looks like the real medicine but does not contain any active ingredients. The study is double blind which means that neither the participants nor the researchers will know who is receiving which treatment during the study. Participants will complete a smell questionnaire called Smell Qx at the start of the study, after 8 weeks of treatment and again at 12 weeks. Each person will be involved in the study for 12 weeks in total.

What are the possible benefits and risks of participating?

Not provided at time of registration

Where is the study run from?

The study will take place at Homerton Healthcare NHS Foundation Trust and James Paget University Hospitals NHS Foundation Trust.

When is the study starting and how long is it expected to run for?
September 2025 to April 2027

Who is funding the study?
Rosetrees Trust (UK)

Who is the main contact?
Andrew Tunstell, a.tunstell@ucl.ac.uk

Contact information

Type(s)
Public

Contact name
Mr Andrew Tunstell

Contact details
University College London
London
United Kingdom
NW1 2PG
+44 20 3447 5369
a.tunstell@ucl.ac.uk

Type(s)
Principal investigator

Contact name
Prof Matt Lechner

Contact details
University College London Division of Surgery and Interventional Science, Charles Bell House, 43-35 Foley Street
London
United Kingdom
W1W 7TS
+44 7535660441
m.lechner@ucl.ac.uk

Type(s)
Scientific

Contact name
Dr Umar Rehman

Contact details
University College London Division of Surgery and Interventional Science, Charles Bell House, 43-35 Foley Street
London

United Kingdom
W1W 7TS
+44 7415345603
U.rehman@ucl.ac.uk

Additional identifiers

Integrated Research Application System (IRAS)
1012783

Protocol serial number
164150

Study information

Scientific Title
Use of gabapentin in the management of post-viral parosmia: a double-blind, randomised, placebo-controlled, multi-site trial

Acronym
COPANOS

Study objectives
Primary objective:
To assess the efficacy of gabapentin treatment in the management of parosmia.
The primary outcome measure will be the difference in the participant reported parosmia symptom severity assessed via the parosmia domain of the Smell Qx survey scores between gabapentin and placebo treated groups following completion of treatment. (Week 8).

The study also aims to find out:
1. Whether gabapentin is safe and well tolerated by people taking it.
2. If gabapentin improves quality of life in people with parosmia.
3. Whether gabapentin improves the sense of smell, based on smell tests.
4. If it reduces the severity of parosmia, as measured by both patient reports and objective parosmia tests.

Ethics approval required
Ethics approval required

Ethics approval(s)
Submitted 16/09/2025, - (-, -, -, United Kingdom; -; -), ref: 25/WA/0298

Primary study design
Interventional

Study design
Interventional double blind randomized parallel group placebo controlled trial

Study type(s)
Efficacy, Safety

Health condition(s) or problem(s) studied
Post-viral Parosmia (distorted smell)

Interventions
This is a double-blind, randomised, placebo-controlled trial investigating the efficacy of gabapentin in the treatment of parosmia. Participants will be randomised in a 1:1 ratio to receive either gabapentin or placebo. Randomisation will be conducted using a computer-generated sequence via Sealed Envelope, employing permuted-block sequencing. Randomisation will be stratified by baseline parosmia severity (Smell Qx parosmia domain), duration of parosmia, age, gender, and Sniffin' Sticks Threshold-Discrimination-Identification (TDI) scores to ensure balance across trial arms.

Active Intervention (Gabapentin): Participants randomised to the active treatment arm will receive gabapentin capsules (300 mg per capsule) administered orally for a total treatment duration of 8 weeks, followed by a weaning phase. The dosing regimen is as follows: Weeks 1–2: one capsule (300 mg) once daily in the evening; Weeks 3–6: one capsule (300 mg) twice daily, every 12 hours (total daily dose 600 mg); Weeks 7–8 (weaning phase): one capsule (300 mg) once daily in the evening. In total, each participant will receive 84 capsules over the treatment course. Dose adjustments are permitted for tolerability: participants experiencing non-serious side effects such as intolerable daytime drowsiness may reduce to 300 mg once daily; additionally, participants reporting subjective symptomatic improvement by Week 2 (based on the Smell Qx parosmia domain) may elect to remain on 300 mg daily rather than escalating to 600 mg daily. Participants will be supplied with medication in two batches: the first at baseline (Visit 1) and the second at Week 3.

Comparator (Placebo): Participants randomised to placebo will receive identically packaged and over-encapsulated placebo capsules, manufactured by Zentiva, matched in appearance, quantity, and dosing schedule to the gabapentin arm. Participants in this arm will follow the same dose-escalation and weaning schedule (Weeks 1–2: one capsule daily; Weeks 3–6: one capsule twice daily; Weeks 7–8: one capsule daily), with the same opportunity for individualised adjustment based on tolerability or subjective improvement, to preserve blinding and procedural equivalence with the active arm.

Follow-Up and Monitoring: Following randomisation, participants will attend clinic visits at baseline (Visit 1), end of treatment (Week 8, Visit 2), and final follow-up (Week 12, Visit 3). Virtual or telephone follow-ups will occur weekly during Weeks 2–6 to monitor treatment compliance, adverse events, and suicidal ideation using the Columbia-Suicide Severity Rating Scale (C-SSRS). At Week 3, participants will attend the pharmacy to collect the remaining study medication, with no additional trial assessments performed at this visit. Adverse event monitoring will occur throughout, including review of patient diaries and pill counts. Safety provisions are in place to discontinue medication in cases of intermediate or high suicide risk, allergic reaction, or intolerable side effects.

This design ensures robust evaluation of gabapentin versus placebo, with identical treatment schedules, dose escalation and weaning phases, compliance monitoring, and blinded assessment of outcomes.

Intervention Type
Drug

Phase

Phase III

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

Primary outcome(s)
Parosmia severity is measured using the Parosmia Domain of the Smell Qx questionnaire (scale 1–5, higher scores = worse severity) at baseline (Week 0), end of treatment (Week 8), and 1-month post-treatment follow-up (Week 12).

Key secondary outcome(s)
1. Parosmia severity is measured using the Parosmia Domain (scale 1–5, higher scores = worse severity) of the Smell Qx questionnaire at baseline (Week 0), end of treatment (Week 8), and follow-up (Week 12).
2. Safety and tolerability are measured by the number and proportion of participants reporting adverse drug reactions, and by responses on the Columbia-Suicide Severity Rating Scale (C-SSRS), at baseline (Week 0), weekly telephone follow-ups during treatment (Weeks 2–6), end of treatment (Week 8), and follow-up (Week 12).
3. Quality of life is measured using the Quality-of-Life Domain of the Smell Qx questionnaire (scale 1–5) at baseline (Week 0), end of treatment (Week 8), and follow-up (Week 12).
4. Olfactory function is measured using the Sniffin' Sticks Threshold-Discrimination-Identification (TDI) test (total score 0–48; <16.5 anosmia, 16.5–30.5 hyposmia, >30.5 normosmia) at baseline (Week 0), end of treatment (Week 8), and follow-up (Week 12).
5. Objective parosmia severity is measured using the Sniffin' Sticks Parosmia Test (SSParoT; Hedonic Range and Hedonic Direction scores) at baseline (Week 0), end of treatment (Week 8), and follow-up (Week 12).

Exploratory Outcomes
1. Cognitive function is measured using the Addenbrooke's Cognitive Examination III (ACE-III; total score 0–100, <77 indicates impairment) at baseline (Week 0) and end of treatment (Week 8).
2. Nasal airflow is measured using peak nasal inspiratory flow, nasal partitioning ratio, tidal volume, double ordinal airway subjective scale, and maximal inhalation flow rate at baseline (Week 0) and end of treatment (Week 8).
3. Taste function is measured using Taste Strips (maximum score 16; <9 hypogeusia, misidentification at highest concentrations = dysgeusia) at baseline (Week 0), end of treatment (Week 8), and follow-up (Week 12).
4. Trigeminal sensitivity is measured by the number of correct lateralisation responses to 40 odour stimuli (benzaldehyde and eucalyptol vs propylene glycol) at baseline (Week 0) and end of treatment (Week 8).
5. Effect of gabapentin dose is measured by comparing Smell Qx Parosmia Domain scores between participants taking 300mg vs 600mg daily at the end of treatment (Week 8)

Completion date
01/04/2027

Eligibility

Key inclusion criteria
1. Participants aged 18–65 years with parosmia secondary to viral infection/COVID-19 infection (≥6 months duration but less than 5 years)

2. Participants must have a Parosmia domain severity score of ≥3/5 on the Smell Qx
3. Participants must have a sniffin stick smell TDI >16.5
4. Participants must be willing able to provide written informed consent
5. Fluent in English and able to understand and complete questionnaires
6. Women of childbearing potential must be willing to use a highly effective method of contraception from consent until end of the trial
7. Female participants of childbearing potential must have a negative urine pregnancy test which will be done at the baseline visit before randomisation and start of trial treatment

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Years

Upper age limit
65 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Participants with known allergies to the odours used in Sniffin Sticks TDI assessment, retronasal olfactory tests or taste strips.
2. Participants with a known allergy to the IMP or its excipients.
3. Parosmia which is primarily associated with chronic sinusitis with or without nasal polyps, allergic rhinitis, sinonasal tumours or other aetiologies.
4. Participants using concurrent medication as listed in Section 8.7. Participants with use of antidepressants/antipsychotics/GABA analogues in the last 12 months.
5. Participants with a history of depression, anxiety, psychosis, self-harm, suicide attempts, or other mental health conditions.
6. Participants who have experienced suicidal or self-harm thoughts within the past month. Participants with any history of neurological conditions e.g. Alzheimer's, Dementia, Parkinsons, Epilepsy, Traumatic Brain Injury or Brain Tumours.
7. Participants with any history of renal failure, dialysis patient, previous renal transplant or known creatinine clearance <30ml/min.*
8. Participants with any history of liver failure, liver disease or previous liver transplant.
9. Participants with a family history of chronic kidney disease, or those currently taking or who have taken a prolonged course (2 weeks or greater) of medications known to affect renal function within the past 6 months, will undergo renal function testing (e.g., creatinine clearance). Medications known to impact renal function include but are not limited too: diuretics such as furosemide, aminoglycosides such as gentamicin, antihypertensives such as ramipril,

nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen, as well as certain antivirals, chemotherapy agents, and calcineurin inhibitors. Individuals with a creatinine clearance of less than 30 mL/min will be excluded from the study. Participants who have comorbidities known to impact renal function such as diabetes, hypertension, cardiovascular disease including previous myocardial infarction, and autoimmune conditions such as systemic lupus erythematosus or rheumatoid arthritis will undergo renal function blood testing. Individuals with a creatinine clearance of less than 30 mL/min will be excluded from the study.
10. Participants with any history of cardiac arrythmias or diagnosed heart failure.
11. Females who are currently pregnant, planning pregnancy or breastfeeding.
12. Participants with a current or any previous addiction to alcohol, cocaine, opiates or any other recreational or prescription medications.
13. Participants operating heavy machinery, working at heights or operating buses/trains/plane /driving long distances.
14. Participants currently involved in, or who have participated within the past 12 months in, any research study involving experimental medications or drug trials.
15. Participants with a diagnosis of cancer who are undergoing active treatment.
16. Participants who are using over-the-counter treatments for olfactory dysfunction, such as vitamin A or omega-3 fatty acids. Participants who are immunocompromised, including those with HIV infection, active malignancy, or currently receiving chemotherapy, immunosuppressive therapy, or long-term corticosteroids, will be excluded from the study.
17. Participants with significant respiratory conditions, such as chronic obstructive pulmonary disease (COPD), severe asthma, or other uncontrolled respiratory diseases, who have required hospitalisation in the past 12 months, require long term oxygen therapy, non-invasive ventilation, long term oral corticosteroids, at home nebulisers or requiring lung surgery will be excluded from the study.
18. Participants with resistant hypertension, defined as uncontrolled hypertension despite requiring an ACE inhibitor or an ARB plus a CCB and a thiazide-like diuretic or under the care of a specialist hypertension clinic, will be excluded.
19. Participants with a history of blood or clotting disorders (e.g. thrombocytopenia, leukaemia) or those taking antiplatelet agents (e.g. aspirin, clopidogrel) will be excluded.

* Creatinine clearance will not be routinely assessed as gabapentin is not reported to be nephrotoxic. It will be evaluated in individuals with:
• Known renal disorders (e.g. glomerulonephritis, nephrotic syndrome)
• Systemic conditions that may affect renal function (e.g. diabetes mellitus, systemic lupus erythematosus, hypertension)
• Use of nephrotoxic medications (e.g. aminoglycosides, Non-steroidal anti-inflammatory drugs (NSAIDs), antihypertensive medications)

Date of first enrolment
13/10/2025

Date of final enrolment
01/03/2027

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Homerton Healthcare NHS Foundation Trust
Homerton Row
London
England
E9 6SR

Study participating centre
James Paget University Hospitals NHS Foundation Trust
Lowestoft Road
Gorleston
Great Yarmouth
England
NR31 6LA

Sponsor information

Organisation
University College London

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type
Charity

Funder Name
Rosetrees Trust

Alternative Name(s)
Rosetrees, Teresa Rosenbaum Golden Charitable Trust

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
On completion of the trial, the data will be analysed and the final trial report will be prepared. Trial participants will be made aware of the trial results following completion and publication of the study, with an online link to the published results provided to participants who request this.

Data sharing
De-identified individual participant data that support the findings of the trial may be made available upon reasonable request, where legally and ethically permissible. Requests for data access should be submitted to the Chief Investigator (Matt Lechner, m.lechner@ucl.ac.uk) and the trial Sponsor. All requests will be reviewed by the study team and Sponsor to ensure that the proposed use is scientifically appropriate, consistent with the terms of ethical approval, and compliant with applicable data protection and confidentiality requirements.

Data will only be shared after appropriate review and approval, and subject to completion of any required data sharing or data transfer agreements. No identifiable participant data will be shared.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		23/07/2026	27/07/2026	Yes	No