

# Are there differences in central nervous system processing in patients with refractory chronic cough?

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<b>Registration date</b> 10/12/2018	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 25/06/2024	<b>Condition category</b> Respiratory	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

Cough is one of the most common conditions for which treatment is sought, but treatment options are very limited. Some people experience chronic cough, which persists despite attempts to treat. This can be very distressing and disruptive to sufferers. It is suspected that these patients suffer from a hyper-sensitivity of the cough reflex, affecting the nerves either in the peripheral or central nervous system (CNS). Some drugs which act on the CNS have been shown to reduce cough in some patients, but not all. The aim of this study is to investigate the CNS by comparing brain activity in chronic cough patient to that of healthy volunteers. Resting-state functional magnetic resonance scanning (fMRI) is used to look at which areas of the brain interact with each other in chronic cough and if this differs from activity seen in healthy volunteers.

### Who can participate?

Healthy volunteers and chronic cough patients, aged between 18 and 80

### What does the study involve?

The study involves two visits for healthy volunteers and three visits for cough patients. Participants are asked to complete some questionnaires about cough and other symptoms they may experience. Their blood pressure, heart rate and oxygen saturation are measured, as are their height and weight. A blood sample and urine sample are taken. Chronic cough patients are asked to wear a cough monitor - a device which records the number of times they cough in 24 hours. This visit takes place at Wythenshawe Hospital, Manchester. All volunteers are asked to complete a cough challenge at Wythenshawe Hospital. This involves inhaling different concentrations of saline which can cause cough. The challenge is stopped when the participant has reached the maximum dose that they can tolerate. Chronic cough patients are asked to complete this after the 24-hour cough monitoring period. Healthy volunteers can complete the challenge as part of the screening visit. Volunteers are asked to attend a visit at the PET-MR unit at St Mary's Hospital, Manchester. A resting-state fMRI scan is carried out. This involves lying in an MRI scanner for 20 minutes, split over two 10-minute sessions, and relaxing without falling to sleep. While the participant is being scanned, their breathing rate and depth are measured using

a respiratory band around the chest, their heart rate is measured, and their blood oxygen levels are measured using a clip on their finger. Their exhaled carbon dioxide is also measured. The day after the scan, the researcher calls the volunteer to make sure that they are well after taking part in the study.

What are the possible benefits and risks of participating?

There are no benefits of participating in the study. All of the research methods have been used many times and only carry minimal risks. Giving a blood sample may be uncomfortable and might leave a small bruise.

Where is the study run from?

Wythenshawe Hospital (UK)

When is the study starting and how long is it expected to run for?

February 2017 to September 2022

Who is funding the study?

Wellcome Trust (UK)

Who is the main contact?

Rachel Dockry

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## Contact information

### Type(s)

Scientific

### Contact name

Dr Rachel Dockry

### Contact details

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## **Additional identifiers**

### **Clinical Trials Information System (CTIS)**

Nil known

### **Integrated Research Application System (IRAS)**

258150

### **ClinicalTrials.gov (NCT)**

Nil known

### **Protocol serial number**

18/CoCen/001, 207504/B/17/Z, IRAS 258150

## **Study information**

### **Scientific Title**

Are there differences in central nervous system processing in patients with refractory chronic cough?

### **Acronym**

Cough Central

### **Study objectives**

Patients suffering from chronic treatment-refractory cough have different brain activity than seen in healthy volunteers.

### **Ethics approval required**

Old ethics approval format

### **Ethics approval(s)**

Approved 11/03/2019, North West - Greater Manchester West Research Ethics Committee (Barlow House, 3rd Floor, 4 Minshull Street, Manchester, M1 3DZ; 0207 104 8021; nrescommittee.northwest-gmwest@nhs.net), ref: 19/NW/0105

### **Study design**

Observational case-control study

### **Primary study design**

Observational

### **Study type(s)**

Other

## **Health condition(s) or problem(s) studied**

Chronic cough

## **Interventions**

Volunteers will be asked to attend a screening visit to determine eligibility for the study. Here their medical history and demographics will be recorded; their blood pressure and heart rate will be measured; and their height and weight will be measured. The volunteer will be asked to complete some questionnaires and perform a spirometry test. If the results of all of these tests show that the subject is suitable, the chronic cough patients will be asked to wear a cough monitor to record their coughing for 24 hours. After the completion of the cough monitoring period, the patient will be asked to return to the clinical trials unit to complete a cough challenge. Healthy volunteers will be asked to complete the cough challenge as part of the screening visit.

A cough challenge involves inhaling increasing doses of an agent which may make the volunteer want to cough. In this case, we are using hypotonic saline. The test continues until the volunteer reached their maximum tolerated dose of saline. Spirometry is performed both before and after the challenge test as a safety precaution.

The final visit involves an MRI scan of the brain. This visit will take around 35 minute and involves the participant lying in the scanner and thinking about nothing for two sessions, 10 minutes each. Whilst in the scanner the volunteers will have their breathing rate measured by a band about their chest, their heart rate and blood oxygen saturation measured by a finger clip and their exhaled carbon dioxide measured by a tube which sits under their nose.

## **Intervention Type**

Other

## **Primary outcome(s)**

Brain connectivity assessed using an fMRI scan at the final visit

## **Key secondary outcome(s)**

All outcomes are only measured once (baseline):

1. Cough frequency, recorded by an ambulatory cough monitor
2. Cough reflex sensitivity, as determined by a cough challenge
3. The impact of cough on daily life and activities, measured using the Cough Quality of Life Questionnaire (CQLQ)
4. Depression, measured using The Centre for Epidemiological Studies depression scale (CED-S)
5. Interoception, measured using The Multidimensional Assessment of Interoceptive Awareness (MAIA)

## **Completion date**

09/09/2022

## **Eligibility**

### **Key inclusion criteria**

1. Males and females 18-80 years, inclusive
2. Non-smokers >6 months; ex-smokers <20 pack years

### Healthy Volunteers

3. No clinically relevant abnormalities based on the medical history, physical examination, vital signs
4. No history of current or significant past respiratory disease, specifically a diagnosis of asthma
5. Spirometry within normal limits

### Chronic Cough Patients

6. Have a refractory chronic cough as defined by BTS guidelines
7. No evidence of asthma

### Participant type(s)

Mixed

### Healthy volunteers allowed

No

### Age group

Adult

### Lower age limit

18 years

### Upper age limit

80 years

### Sex

All

### Total final enrolment

74

### Key exclusion criteria

1. Routine contraindications to fMRI scanning e.g. certain metal implants, recent surgery, extreme claustrophobia etc
2. Any condition that may increase airway/circulating levels of ATP/adenosine e.g. chronic cardiac failure, chronic hypoxia, vigorous exercise within 48 hours
3. Pregnant or breastfeeding
4. Upper or lower respiratory tract infection or significant change in pulmonary status within 4 weeks of enrolment
5. Any therapy that may modulate cough (e.g. ACE inhibitors, opioids, gabapentin). Patients can be included if they are willing/able to discontinue these for the study duration and a suitable washout period

### Date of first enrolment

01/02/2020

### Date of final enrolment

02/09/2022

# Locations

## Countries of recruitment

United Kingdom

England

## Study participating centre

### MFT Wythenshawe Hospital

Southmoor Road

Wythenshawe

Manchester

United Kingdom

M23 9LT

# Sponsor information

## Organisation

Wythenshawe Hospital Research and Development Directorate

## ROR

<https://ror.org/05vpsdj37>

# Funder(s)

## Funder type

Research organisation

## Funder Name

Wellcome Trust

## Alternative Name(s)

## Funding Body Type

Private sector organisation

## Funding Body Subtype

International organizations

## Location

United Kingdom

# Results and Publications

## Individual participant data (IPD) sharing plan

The data sharing plans for the current study are unknown and will be made available at a later date.

## IPD sharing plan summary

Data sharing statement to be made available at a later date

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">HRA research summary</a>			28/06/2023	No	No