# Assessing the effects of smell training on the brains of patients with an impaired sense of smell after surgery

Submission date	Recruitment status	Prospectively registered
30/05/2020	No longer recruiting	Protocol
Registration date	Overall study status	Statistical analysis plan
02/06/2020	Completed	Results
Last Edited	Condition category	Individual participant data
02/06/2020	Ear, Nose and Throat	<ul><li>Record updated in last year</li></ul>

# Plain English summary of protocol

Background and study aims

Olfactory dysfunction is the inability to perceive smells. Its treatment is challenging due to limited therapeutic options. Olfactory training has been shown to improve smell identification, discrimination, and the threshold for odour detection of patients with olfactory dysfunction with postinfectious etiology (i.e. after an infection). The aim of this study is to assess the effect of olfactory training in patients with olfactory dysfunction after pituitary surgery (post-surgical etiology) using functional magnetic resonance imaging (fMRI scan) to see if it induces neural (brain) reorganization processes.

## Who can participate?

Patients with post-surgical olfactory dysfunction lasting for at least 1 year after endoscopic transsphenoidal pituitary surgery

## What does the study involve?

Participants undergo an examination that includes a nasal endoscopic evaluation. They are also tested using an olfactory measurement test (Sniffing Stick test) and undergo an fMRI scan. Participants are randomly allocated to undergo olfactory training for 12 weeks or no treatment. Olfactory training is performed using four essential oils. Participants are instructed to expose themselves twice a day to each odour taking deep sniffs for 30 seconds and resting 10 seconds between each oil. Additionally, they are instructed to evoke a memory or feeling during the odour exposure that is associated with the smell of the essential oil. Participants are contacted monthly to maintain compliance and motivation during the training period. At the end of the 12-week training period, both groups are assessed using the olfactory performance test and fMRI, and the control group receive olfactory training.

What are the possible benefits and risks of participating?

The possible benefits are the partial or complete recovery of olfactory function after olfactory training. This study does not have any risks for the participants.

Where is the study run from? Pontificia Universidad Catolica de Chile (Chile)

When is the study starting and how long is it expected to run for? May 2017 to May 2021

Who is funding the study? Fondo Nacional de Desarrollo Científico y Tecnológico (Chile)

Who is the main contact? Dr Francisco García-Huidobro fggarciahuidobro@uc.cl

# Contact information

# Type(s)

Scientific

#### Contact name

Dr Francisco Garcia-Huidobro

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# Additional identifiers

# Clinical Trials Information System (CTIS)

Nil known

# ClinicalTrials.gov (NCT)

Nil known

## Protocol serial number

170728010

# Study information

### Scientific Title

Neuroplasticity assessment using fMRI after olfactory training in post-surgical olfactory impaired patients

## Acronym

#### **NOTFMRI**

## **Study objectives**

Olfactory training will induce neuroplasticity processes on associated olfactory areas in patients with post-surgical olfactory dysfunction.

## Ethics approval required

Old ethics approval format

## Ethics approval(s)

Approved 05/09/2017, the scientific ethics committee of Pontificia Universidad Catolica medical faculty (Marcoleta 381 – fourth floor, Office 42, Santiago, Chile; +562 (0)23548173; Cecmeduc@med.puc.cl), ref: 170728010

# Study design

Single-center interventional randomized controlled trial

## Primary study design

Interventional

## Study type(s)

**Treatment** 

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

Post-surgical olfactory dysfunction

#### **Interventions**

All participants undergo an olfactory measurement test to diagnose olfactory dysfunction and assess severity. Also, they are examined by an ENT specialist's including a complete physical exam and nasofibroscopy, to exclude other conditions that could be causing smell impairment. For the scanning sessions, an odour infusion system is attached to a single air-line, to perform the sniffing paradigm, which is characterized by an odour intake of eucalyptus essential oil through a nasal cannula.

Also, a trigeminal activation paradigm is performed to assess the indemnity of the trigeminal system, characterized by the intake of odourless CO<sub>2</sub> through a nasal cannula. After the first fMRI and olfactory performance assessment, the smell-impaired cohort is randomized into two groups. Participants are randomized by simple randomization using computer-generated random numbers. The allocation is concealed from the research team. No masking is used.

Intervention: Olfactory training for 12 weeks

Control: No treatment

Olfactory training is performed using four essential oils: lemon (limonene 67.08% and b-pinen 12.52%), eucalyptus glovus (1-8-cineole 60%), clove (eugenol 75.49% and eugenol acetate 13.59%) and lavender (linalool 36.53% and linalyl acetate 32.80%). Patients are instructed to expose themselves twice a day to each odour taking deep sniffs for 30 seconds and resting 10 seconds between each oil. Additionally, they are instructed to evoke a memory or feeling during the odour exposure that is associated with the smell of the essential oil. Patients are contacted monthly to maintain compliance and motivation during the training period.

At the end of the 12-week training period, both groups are assessed using olfactory performance test and fMRI, and the control group receive olfactory training.

## Intervention Type

Other

## Primary outcome(s)

Activation areas and functional connectivity during olfactory stimulation measured using functional MRI images before olfactory training and 12 weeks after the intervention

## Key secondary outcome(s))

Olfactory function assessed using olfactometric measurements before olfactory training and 12 weeks after the intervention

## Completion date

01/05/2021

# Eligibility

## Key inclusion criteria

- 1. Referred post-surgical olfactory dysfunction lasting for at least 1 year
- 2. Only patients with a definite diagnosis of olfactory dysfunction were finally included
- 3. No history of psychiatric or neurodegenerative diseases

## Participant type(s)

**Patient** 

## Healthy volunteers allowed

No

## Age group

Adult

#### Sex

Αll

## Key exclusion criteria

- 1. Olfactory dysfunction not related to surgical procedures
- 2. Associated psychiatric or neurodegenerative diseases
- 3. Pediatric age

## Date of first enrolment

01/10/2017

## Date of final enrolment

31/12/2020

# Locations

#### Countries of recruitment

Study participating centre Pontificia Universidad Catolica de Chile

Marcoleta 352 Santiago Chile 8330033

# Sponsor information

## Organisation

Pontifical Catholic University of Chile

## **ROR**

https://ror.org/04teye511

# Funder(s)

# Funder type

Government

## **Funder Name**

Fondo Nacional de Desarrollo Científico y Tecnológico

# Alternative Name(s)

National Fund for Scientific and Technological Development, El Fondo Nacional de Desarrollo Científico y Tecnológico, FONDECYT

# Funding Body Type

Government organisation

# Funding Body Subtype

National government

#### Location

Chile

# **Results and Publications**

# Individual participant data (IPD) sharing plan

The data that is stored are the demographic data of each patient, the olfactometric results and the fMRI images of each of the patients. This data is private and the ethics committee only authorizes its use by the authors for scientific publication protecting the anonymity of the participants. There are no web links available, and data is stored in the Bioimaging center of the University.

## IPD sharing plan summary

Stored in repository

## **Study outputs**

Output type Details Date created Date added Peer reviewed? Patient-facing?

Participant information sheet 11/11/2025 No Yes