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Study of brain activity in misophonia and the effect of cognitive behavioral therapy

Submission date
11/10/2016

Recruitment status
No longer recruiting

Registration date
28/10/2016

Overall study status
Completed

Last Edited
16/07/2019

Condition category
Mental and Behavioural Disorders

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[X] Results
[ ] Individual participant data

Plain English summary of protocol

Background and study aims
Misophonia is a newly defined mental health condition in which hearing specific sounds provoke intense aggression and disgust. Ordinary sounds that people make, such as lip-smacking and breathing, cause patients with misophonia to become suddenly aggressive and feel agitated. This can be so intense that they also often develop time-consuming strategies to avoid hearing these sounds. The suffering and avoidance lead to major social and work-related impairment. Little is known about the underlying causes or mechanisms of misophonia. In addition, there is currently no evidence-based treatment available. Cognitive behavioural therapy (CBT) is a type of talking therapy which helps people to change the way they think and behave. The aim of this study is to investigate the underlying mechanisms for misophonia in the body and find out whether CBT can be an effective treatment.

Who can participate?
Adults with misophonia and healthy adults of the same age.

What does the study involve?
Individuals with misophonia are interviewed and put on a waiting list before treatment. The treatment involves 10 weeks of weekly group therapy which last for four hours per day. Therapy consists of CBT and psychomotor therapy (a type of treatment that uses body awareness and physical activities) techniques. Patients are instructed to practice at home between the treatment sessions. At the start of the study, midway through treatment, after finishing treatment and then 18 weeks after finishing treatment), patients fill out questionnaires to find out if their symptoms and general mental state have changed.
In another part of the study, patients from the first part of the study and healthy adults of the same age undergo brain scans on two occasions (at the start of the study and after 10 weeks). This involves having their brain activity measured when completing a range of activities and watching videoclips that are intended to trigger the symptoms of misophonia. Participants also provide blood samples at the start of the study and after 10 weeks in order to assess whether there is a genetic basis for misophonia.

What are the possible benefits and risks of participating?
Individuals with misophonia benefit from receiving therapy which could help reduce their misophonia symptoms. There is a small risk of pain or bruising when having blood samples taken.

Where is the study run from?
Academic Medical Center (Netherlands)

When is the study starting and how long is it expected to run for?
July 2011 to April 2016

Who is funding the study?
Academic Medical Center (Netherlands)

Who is the main contact?
Mrs Arjan Schroder

Contact information

Type(s)
Public

Contact name
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Additional identifiers

Protocol serial number
NL37726.018.11

Study information

Scientific Title
Misophonia: An imaging study on the neurobiology and the efficacy of cognitive behavioural therapy

Study objectives
Study aims:
1. To identify differences in functional activation of the brain between patients with misophonia and normal controls, using 1. functional magnetic resonance imaging (MRI) and 2. Electroencephalography (EEG) to prove the following hypotheses:
1.1. Hypoactivation of prefrontal regions in misophonia patients
1.2. Limbic, especially amygdalar, hyperactivation in patients following misophonic stimuli
2. To assess efficacy of cognitive behavourial therapy (CBT) and psychomotor therapy (PMT) in

patients with misophonia, using psychiatric questionnaires and neuroimaging to prove the following hypotheses:
2.1. There will be a decrease in misophonia symptoms after CBT/PMT and an increase in psychosocial functioning
2.2. On the functional activation of the brain in patients with misophonia we expect the following:
2.3. The anticipation of increased activation of the medial and/or orbital prefrontal cortex post-treatment.
2.4. The anticipation of decreased activation of the amygdala post-treatment
3. To perform genetic analysis in order to find a genetic cause of misophonia to prove the following hypotheses:
3.1. Candidate chromosomal regions or genes will be found which probably can lead to a genetic clarification for misophonia
3.2. In case of a significant decrease of symptoms and increase of psychosocial functioning in patients after therapy significant epigenetic changes will be found which could confirm the effect of therapy

Ethics approval required
Old ethics approval format

Ethics approval(s)
Medical Ethics Review Committee of the Academic Medical Center, 16/01/2012, ref: NL37726.018.11

Study design
Open-label non-randomised study

Primary study design
Interventional

Study type(s)
Treatment

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

Interventions
All patients will receive cognitive behavioral therapy (CBT) and psychomotor therapy (PMT) in a group, on a weekly basis during 10 weeks. The CBT/PMT program follows a strict standardized protocol for treatment in a group. The duration of treatment is 10 weeks, with weekly sessions. The group size will be 8 patients maximum. Each therapy day offers the patients a four-hour program of CBT and PMT, which consists of aggression regulation, task concentration training, applied relaxation, counter conditioning and stimulus exposure. The target of treatment of misophonia is to decrease the aggression related to misophonic sounds, by disconnecting the aggression from the misophonic sound, by lowering irritability and by increasing the sense of self-control.
Participants will be followed up midway through treatment (5 weeks), after treatment (10 weeks) and 18 weeks after finishing treatment (28 weeks). This involves assessment of misophonia symptom severity and general mental state using different questionnaires.

fMRI sub-study:
A sub-sample of participants from the main study will participate in the MRI study. Structural scans (T1 weighted, DTI) will be taken. In the functional MRI paradigm participants will then be exposed to videoclips and sounds depicting aversive misophonia preducing sounds, like someone eating, lip-smacking or breathing heavily whilst undergoing fMRI scanning. This will be mixed with blocks with neutral videoclips and sounds. Both neutral and misophonia conditions will consist of 6 blocks each, duration 20 seconds. fMRI scanning takes place before the start of treatment (T0) and after finishing treatment (T+10) at the Brain Imaging Center (BIC) of the AMC.

Intervention Type
Behavioural

Primary outcome(s)
1. Misophonia symptom severity is measured with the Amsterdam Misophonia Scale (A-MISO-S) and Clinical Global Impression Scale (CGI) at first interview at baseline, 5, 10 and 28 weeks
2. Cortical brain activity is measured using Electroencephalography (EEG), using an auditory mismatch negativity (MMN) paradigm, at baseline and 10 weeks
3. Genetic clarification for misophonia and the effect of treatment is assessed using DNA samples, which will be collected for epigenetic analysis in patients by peripheral blood samples taken at baseline and 10 weeks

fMRI study:
1. Change in BOLD activation in patients will be measured at baseline (before treatment) and week 10 (after treatment)
2. Differences in BOLD activation between patients and controls will be examined at baseline and week 10

Key secondary outcome(s))
1. Anxiety and depression symptoms will be assessed using the Hamilton Anxiety Rating Scale (HARS) and Hamilton Depression Rating Scale (HDRS) at first interview at baseline, 5, 10 and 28 weeks
2. Psychopathology will be measured using the Symptom Checklist (SCL-90R) at first interview at baseline, 5, 10 and 28 weeks
3. Social avoidance and aggressiveness will be assessed with the Inventarisatielijst Omgaan met Anderen (IOA) and Agressie Vragenlijst (AVL) at first interview at baseline, 5, 10 and 28 weeks

Completion date
04/04/2016

Eligibility

Key inclusion criteria
Patient inclusion criteria:
1. Meet the diagnostic criteria for misophonia, as proposed by Schröder and Denys
2. Male and female, aged above 18 years
3. Female patients of childbearing potential must have a negative pregnancy test and use reliable method of contraception
4. Written informed consent
5. Eligible for exposure therapy

Healthy control inclusion criteria:
1. Age between 18 and 65
2. Subjects have signed informed consent in accordance with the provisions of the pertinent excerpt from the Declaration of Helsinki (October, 2000) and Dutch legal regulation (Wet Medisch Wetenschappelijk Onderzoek met Mensen).
3. No current or past psychiatric disorders

For the fMRI study an additional criterion has been established:
Age between 18 and 65

Participant type(s)
Mixed

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Presence of any of the following DSM IV conditions:
1.1. Major depression
1.2. Major anxiety disorder
1.3. Bipolar Disorder
1.4. Autism Spectrum Disorders
1.5. Schizophrenia or any other psychotic disorder
1.6. Substance related disorder during the past 6 months
1.7. Epilepsy or any structural CNS disorder of stroke within the last year
2. Evidence of clinically significant and unstable cardiovascular, gastrointestinal, pulmonary, renal, hepatic, endocrine or haematological disorders, glaucoma, myocardial infarction within the past year or micturition abnormalities
3. Currently taking benzodiazepines, antidepressants or stimulants
4. Patients at risk for suicide
5. Inability to speak Dutch or English

For the fMRI study four additional criteria have been established:
1. Ferrous objects in or around the body (e.g. braces, glasses, pacemaker, metal fragments)
2. Drug or alcohol abuse over a period of six months prior to the experiment
3. History of closed-head injury
4. Patients with claustrophobia

Date of first enrolment
18/04/2012

Date of final enrolment

30/06/2015

Locations

Countries of recruitment
Netherlands

Study participating centre
Academic Medical Center
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Sponsor information

Organisation
Academic Medical Center

ROR
https://ror.org/03t4gr691

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Academisch Medisch Centrum

Alternative Name(s)
Academic Medical Center, AMC

Funding Body Type
Private sector organisation

Funding Body Subtype
Universities (academic only)

Location
Netherlands

Results and Publications

Individual participant data (IPD) sharing plan

The current 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?
Results article	fMRI substudy results	01/12/2019	16/07/2019	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes