Understanding Hallucinations (part II) - fMRI & EEG

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON45084

Source
ToetsingOnline

Brief title
Understanding Hallucinations 2

Condition

- Other condition

Synonym
Hallucinations, illusory perceptional experience

Health condition

Op het symptoom van hallucinaties in 6 verschillende diagnostische groepen: schizofrenie, Ziekte van Parkinson, Ziekte van Alzheimer, Lewy body dementie, patiënten die slechtziend zijn en patiënten die slechthorend zijn.

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: - EEG, - fMRI, - hallucinations

Outcome measures

Primary outcome

The main study endpoints are differences between hallucinating and non-hallucinating participants and between hallucinating individuals of different subtypes in:

- resting state correlates as measured with fMRI, namely: connectivity within the DMN and connectivity of the DMN to sensory cortices and the hippocampal-amygdala complex.
- EEG spectral analysis, synchronization likelihood, clustering index, path lengths and assortativity.
- auditory and visual cortex synchronized burst activations.

Secondary outcome

n.a.

Study description

Background summary

Many people experience an auditory or visual percept in the absence of adequate environmental stimuli, i.e. hallucinations, although they suffer from quite different diseases. In schizophrenia, the vast majority of patients experience

hallucinations and some 25% of them fail to respond to antipsychotic medication (Sommer et al. 2012). Schizophrenia patients facing chronic hallucinations experience severely impaired quality of life and increased risk for suicide and violence (Hor and Taylor 2010). Hallucinations frequently remain undiagnosed and untreated in these patients (Brewin and Patel, 2010). Between 12 and 35% of patients with visual loss develop hallucinations; the Charles Bonnet syndrome (CBS) (Teunisse et al. 1996), from whom 28% are severely distressed by their hallucinations (Teunisse et al. 1996). In patients with hearing loss, auditory hallucinations can occur; the auditory equivalent of CBS (Teunisse et al. 2012). Hallucinations occur in approximately one-third of Parkinson's disease (PD) patients (Fénelon and Alves 2010).
Hallucinations are currently treated in accordance to guidelines for the underlying diagnostic entity. However, one subtype of hallucinations may occur in several different disorders, while patients with the same diagnosis may experience different subtypes of hallucinations. These subtypes may result from different neuropathology and may be responsive to different treatment strategies. Identification of the neuropathological origin of these subtypes of hallucinations may improve prediction of treatment response and stimulate the development of new treatment strategies.
To summarize, hallucinations are common and often stressful in all of the above disorders, while treatment for hallucinations is far from optimal (Sommer, Koops, & Blom, 2012). It is currently not possible to predict treatment response in individual patients and pharmacotherapy is therefore based on trial-and-error. At this point, we do not understand the complete pathophysiological mechanism of hallucinations, but some factors associated with hallucinations in particular diagnoses have been well established (Meppelink et al., 2009; Meppelink, de Jong, van der Hoeven, & van Laar, 2010; Sommer et al., 2008; Sommer et al., 2012). To associate different phenomenological subtypes of hallucinations with different pathophysiological mechanisms can help to make rational treatment decisions on an individual basis and enhance the development of innovative treatment paradigms.

Study objective

The primary objectives of this proposal are:

- to reveal specific abnormalities on resting state fMRI activity of the DMN and connectivity between DMN, medial temporal lobe structures and perceptual cortices related to the pathophysiology of different subtypes of hallucinations
- to examine the frequency of spontaneous synchronized burst activations in auditory and visual cortices using fMRI.
- Reveal resting state EEG correlates (spectral analysis, synchronization likelihood) related to the pathophysiology of different subtypes of hallucinations.
- Reveal correlating patterns of EEG and fMRI that underlie the experience of hallucinations across different disorders.

Study design

In the proposed study, we intend to examine neural correlates of hallucinations over different disorders using resting state EEG, and fMRi in an observational study.
A total of 325 participants will be included: 25 hallucinating participants per diagnostic group and a control group. The control group will consist of 175 non-hallucinating individuals who have the same disorder as the hallucinating individuals and are matched group-wise for severity of the disease, medication, age, sex, handedness and education to minimize differences between groups that may confound study results. Extensive diagnostic screening of the hallucinations will already have been completed for all participants in the previous study Understanding Hallucinations * Part 1 (13-059).
For each subject, an MRI scan of 40 minutes duration and an EEG scan of 5 minutes duration will take place. Including preparation time for the scan and EEG, this visit will have a duration of 2,5 hours. All measurements will be conducted at the University Medical Center in Utrecht.

Study burden and risks

An important benefit is that understanding the underlying pathophysiology of different subtypes of hallucinations may enable rational selection of the most adequate type of treatment on basis of the phenomenology of the patient's hallucinations. Moreover, the outcome measures of the current study may help to predict treatment response so that the risk of severe side-effects need not be taken in the predicted non-responders.
In schizophrenia patients, hallucinations fail to respond to any type of medication in 25% (Shergill, Murray, & McGuire, 1998). As schizophrenia is a common and life-long disorder, a high number of schizophrenia patients currently face chronic hallucinations. Understanding the genesis of (subtypes of) hallucinations will provide new leads for treatment in all these patient groups who can currently not be helped. If this project indicates that decreased attention is an important mechanism in all or in some subtypes of hallucinations, treatment to increase attention can be effective. Furthermore, uncovering the exact pathophysiology of (subtypes of) hallucinations will provide important knowledge for patients, their family and society. A clear explanation on the genesis of hallucinations helps the patient understand what is going on. Understanding the neural substrate of hallucinations will help family and society to understand these experiences and decrease stigmatisation of people with hallucinations, which facilitates their social reintegration.
Another benefit is that research into subtypes of hallucinations is bound to enrich our understanding of perception, similar to how research into subtypes of aphasia has vastly increased our understanding of the language system.

The risk to participants is considered minimal, while the potential benefits are considerable. Undergoing an fMRI scan and EEG recordings may lead to

additional anxiety and/or fatigue in some patients. These risks are considered to be reasonable and minimal. As the potential benefits in terms of knowledge gained are quite large, the benefits clearly outweigh the risks.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Previous participation in the phenomenology/cognition study 13-059.
- Belong to one of the following diagnostic groups:
1.Patients with schizophrenia
2. Patients with Parkinson's disease
3. Patients with Lewy body dementia
4. Patients with Alzheimer's disease
5. Patients with hearing impairment

6.Patients with visual loss
- Written informed consent

Exclusion criteria

- < 18 years of age
- Any contraindication for a 3Tesla MRI scan

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	07-12-2013
Enrollment:	325
Type:	Actual

Ethics review

Approved WMO Date:	23-10-2013
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	20-12-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL43800.041.13