The Iris + study: advanced MRI of the brain in changes of behavior

Published: 14-10-2011
Last updated: 29-04-2024

The purpose of this study is to assess whether measures acquired with advanced MRI neuroimaging can be used to differentiate between bvFTD phenocopy patients and healthy controls. For each technique the research question is listed below:1 -...

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

Summary

ID

NL-OMON41574

Source
ToetsingOnline

Brief title
IRIS +

Condition

- Other condition

Synonym
bvFTD phenocopy patients

Health condition

neurodegeneratieve of neuropsychiatrische aard

Research involving
Human

Sponsors and support

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

Intervention

Keyword: -activation, Behavioral variant frontotemporal dementia, Brainintegrity, MRI, -perfusion, Phenocopy syndrome

Outcome measures

Primary outcome

* White and grey matter volumes.

* White matter integrity: mean diffusivity (MD) and fractional anisotropy (FA)

maps.

* Brain activity: extent of fMRI activation (number and spatial distribution of

significantly activated voxels).

* Quantitative brain perfusion maps.

Secondary outcome

na

Study description

Background summary

The second most common type of presenile dementia after Alzheimer*s disease is frontotemporal dementia (FTD). Its prevalence is estimated to be 2.7/100,000 inhabitants in the Netherlands (Rosso et al., 2003). The most common presentation of FTD is the syndrome characterized by progressive deterioration in social and personal conduct (Neary et al., 1998), also referred to as behavioral-variant FTD (bvFTD). Current diagnostic criteria are based on clinical features such as behavioral disinhibition, apathy or inertia, loss of sympathy or empathy and behavior that is perseverative, stereotyped or compulsive. Hyperorality and dietary changes may also occur. The neuropsychological profile is often characterized by executive dysfunction with

relative intact memory and visuospatial function (Rascovsky et al., 2007). Striking is the patient*s lack of insight into or the concern for his or her actions (McKhann et al., 2001) The underlying neuropathological changes found post mortem all concern atrophy of the bilateral frontotemporal lobes (Piguet, Hornberger, Mioshi, & Hodges, 2010). Surprisingly, in a subset of patients with a clinical diagnosis of bvFTD, this focal atrophy is not found using structural magnetic resonance imaging (MRI) (Kipps et al., 2007). For that reason, MRI findings have until now only remained supportive in the eventual diagnosis of FTD (McKhann et al., 2001; Neary et al., 1998). However, interest in this group of patients with normal MRI despite a clinical bvFTD diagnosis has recently increased as the absence of MRI abnormalities has been associated with a more benign disease course than in patients with MRI abnormalities: whereas the majority of patients with frontotemporal atrophy were dead or institutionalized within 3 years, patients with no or borderline atrophy survived more than 9 years to institutionalization or death (Davies et al., 2006). This observation has given rise to the debate whether these patients, despite fulfilling the bvFTD diagnostic criteria, actually suffer from an underlying neurodegenerative condition (Kipps, Hodges, & Hornberger, 2010). Such patients are therefore considered to have the bvFTD *phenocopy* syndrome, i.e. presenting with the characteristic behavioral features of bvFTD without progressing to actual dementia.

Until now it remains unclear whether the etiology of the phenocopy bvFTD is neurodegenerative or neuropsychiatric. One can assume however, given the typical changes in these patients on a behavioral level, that changes are also taking place on a neurophysiological level. Recent studies attempted to detect these changes by in vivo imaging methods as structural MRI and positron emission tomography (PET). As mentioned before, MRI scans of these patients do not reveal any atrophy on MRI (Davies et al., 2006; Kipps et al., 2007) or abnormal metabolism on PET scans (Kipps et al., 2009). For that reason, more advanced neuroimaging techniques such as functional MRI (fMRI), resting state fMRI, diffusion tensor imaging (DTI) and arterial spin labeling (ASL) may be necessary to detect more subtle neurophysiological processes than changes in volume and metabolism as found by MRI and PET, that can provide insight as to why these patients are so severely impaired in social and interpersonal conduct. With functional MR imaging (fMRI), activity of the brain can be measured noninvasively. Brain activation during performance of cognitive tasks that are associated with clinically affected domains may reveal differences in bvFTD phenocopy patients and controls. Functional MRI can also be acquired when the subject is not performing a task, i.e. at rest, to visualize brain activity in the resting state (resting state fMRI). Spontaneous or baseline brain activity measured by this type of imaging may differ between patients and controls. With diffusion tensor imaging (DTI) the microstructure of the grey and white matter can be assessed noninvasively. An increase of mean diffusivity (MD) and reduction of fractional anisotropy (FA) may indicate loss of parenchymal integrity, occurring prior to actual brain volume loss.

Arterial spin labelling (ASL) is a non-invasive MR imaging technique with which brain perfusion can be measured quantitatively. ASL has several advantages over

PET and SPECT imaging, in terms of its non-invasiveness, higher spatial and temporal resolution and quantitative properties. Its enhanced sensitivity may pick up on changes in perfusion not found by PET.

Study objective

The purpose of this study is to assess whether measures acquired with advanced MRI neuroimaging can be used to differentiate between bvFTD phenocopy patients and healthy controls. For each technique the research question is listed below:
1 - diffusion tensor imaging (DTI):
Do bvFTD phenocopy patients have different mean diffusivity (MD; increase) and fractional anisotropy (FA; decrease) of (normal appearing) white matter compared to healthy controls?
2 - functional MR imaging (fMRI):
Do bvFTD phenocopy patients have different patterns of brain activation during the performance of cognitive tasks that are associated with clinically affected domains compared to controls?
3 - resting state fMRI
Do bvFTD phenocopy patients have different patterns of brain activation during rest compared to controls?
4 - arterial spin labeling (ASL):
Do bvFTD phenocopy patients have different brain perfusion compared to healthy controls?

Study design

Case-control study

Study burden and risks

No permanent hazardous effects of exposure to a static magnetic field as used in MR imaging have yet been demonstrated. Participants will be extensively screened for contraindications by an experienced researcher upon inclusion in the study.

Contacts

Public
Erasmus MC, Universitair Medisch Centrum Rotterdam

's Gravendijkwal 230
Rotterdam 3015 CE
NL
Scientific

Erasmus MC, Universitair Medisch Centrum Rotterdam

's Gravendijkwal 230
Rotterdam 3015 CE
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Patients:
- Age between 40 and 75
- Prominent behavioral changes interfering with social functioning and consisting of disinhibiton and/or apathy and/or stereotypy.
- Patients* initial condition remains stable (i.e. no progression is reported one year after initial routine diagnostic workup).
Control inclusion criteria:
- Age between 40 and 75

Exclusion criteria

Patient exclusion criteria:
- Contraindications for MRI scanning (see appendix for full MRI contraindication screening list)
- Inability to comprehend fMRI tasks
- Psychiatric symptoms
- Dagnosis of dementia
- Acute onset of symptoms
- No heteroanamnesis
- History of cerebral disorders with residual symptoms
- Mental retardation, developmental disorder
- Past or current substance abuse

Control exclusion criteria:
- Contraindications for MRI scanning (see appendix for full MRI contraindication screening list)
- Inability to comprehend fMRI tasks
- Neurocognitive disorders

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	20-10-2011
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO Date:	14-10-2011
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	01-06-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO Date:	02-11-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL36992.078.11