Neuroimage in patients with Breast Implant Illness (BII), an explorative pilot fMRI-study

Published: 21-04-2020
Last updated: 10-04-2024

The aim of this pilot study is to explore the structure and function of brain regions associated with the pain matrix in Breast Implant Illness (BII). This pilot study will be the foundation for grant application for future research.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Observational non invasive

Summary

ID

NL-OMON55243

Source
ToetsingOnline

Brief title
Neuroimage in Breast Implant Illness

Condition

- Other condition
- Autoimmune disorders
- Cognitive and attention disorders and disturbances

Synonym
ASIA-syndrome, breast implant illness

Health condition

pijnregulatie

Research involving

Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht
Source(s) of monetary or material Support: Ministerie van OC&W,Brains Unlimited Pioneer Fund (SWOL),SWOL brains unlimited pioneer fund

Intervention

Keyword: ASIA, Breast implants, fMRI, Silicone

Outcome measures

Primary outcome

Main study parameters/endpoints:

1. The presence of complaints defined as the typical ASIA manifestations (table

1);

Secondary outcome

Secondary study parameters/endpoints

1. Baseline characteristics: age, BMI, education, occupation, duration of

silicone exposure

2. Pain severity, measured with the Chronic Pain Grade 31.

3. Cognitive impairment, measured with MMSE 32

4. Structural MRI (including gray matter volume)

5. Psychosocial health, measured with 4DKL

6. Resting-state fMRI (rs-fMRI) - intrinsic connectivity of the brain in

the resting basal state

7. Diffusion Tensor Imaging (DTI) - Fractional anisotropy (FA)

Study description

Background summary

In 2018, over 1.8 million breast augmentations were performed worldwide. An estimated 3 percent of the Dutch women between 20 and 70 years has breast implants1. Some of these women report a pattern of systemic health complaints with varying severity, such as myalgia, arthralgia, fever, fatigue, dry eyes and mouth, as well as cognitive impairment2, 3. In 1994, Shoaib and Patten described an adjuvant breast neurological disease in patients with silicone breast implants with symptoms of a multiple sclerosis (MS)-like syndrome and/or atypical motor neuron disease4, 5. It is characterized by a collection of neurological symptoms and/or demyelination supposedly caused by silicone breast implants6. In 2011, Shoenfeld et al. introduced ASIA syndrome: an Autoimmune Syndrome Induced by Adjuvants, e.g. breast implants7. Many studies have investigated the possible health effects of silicone breast implants, however, a clear association between breast implants and systemic diseases or autoimmune diseases remains uncertain8-10.
Colaris et al. described a Dutch cohort of ASIA-syndrome patients. Of these women, 98 suffered from fatigue, 91 from arthralgia, 54 from myalgia, 73 from sicca complaints and 20 from severe neurological manifestations. Interestingly, 54 patients underwent removal of their silicone implants, after which 50% of the patients experienced improvement of complaints3.

The explanation of complaints in these patients is probably multi-factorial. In addition to the symptoms that would have occurred in the same person even if no implants were placed, immunogenetic factors, such as pre-existing allergies, and environmental aspects, such as smoking, may play a role in the development of SBI-induced health complaints, also referred to as breast implant illness (BII)11, 12. Furthermore, there is a remarkable overlap with fibromyalgia and it cannot be excluded that it concerns the same disease13-15.

For several decades, fibromyalgia has been recognized as a chronic, centrally mediated, widespread, chronic pain syndrome that affects approximately 2*4% of the population16 17, 18. Ceko et al. also reported that additional to chronic pain, many patients with fibromyalgia complain of problems with memory and concentration19. These cognitive difficulties associated with chronic pain are especially so-called *fibro-fog* in fibromyalgia16, 20. Many fibromyalgia patients experience the cognitive symptoms as more disabling than their chronic pain21.

Previous (functional) MRI studies in chronic pain patients and fibromyalgia patients demonstrated altered brain activity and even structural changes in particular the pain matrix (thalamus, insular cortex, primary somatosensory cortex, secondary somatosensory cortex, anterior cingulate cortex, prefrontal cortex)22-24.

Functional magnetic resonance imaging (fMRI) provides an indirect measurement of brain activity via the blood oxygen level-dependent (BOLD) response, which is a measure of the amount of deoxygenated blood and blood volume in brain regions involved in the response to a stimulus 26. Resting-state functional magnetic resonance imaging (rs-fMRI) examines intrinsic connectivity of the brain in the resting basal state. This technique detects change in terms of the relative levels of oxyhemoglobin and deoxyhemoglobin due to activation of neurons which causes a hemodynamic response27.

DTI (diffusion tensor imaging) is used to map white matter tracts as well as imaging functionally localized brain regions to increase understanding of brain networks and their connectivity. In FM patients, DTI shows decreases in FA (fractional anisotropy) in thalamus and insula and increases in the postcentral gyrus (S1) suggesting more and less effective information transfer, respectively22.
Structural MRI is used for detailed information about gray and white matter. Changes in gray matter volume are often seen in chronic pain/FM (abnormality in PFC, insula, and ACC)22, 23, 25.
In fibromyalgia, connectivity between the insula to the default mode network (DMN) is associated with spontaneous pain (= PFC, ACC and posterior parietal cortex)24.
In FM, increased activation of the insula correlated with pain intensity, decreased activation of DLPFC correlated with poor coping during pain22, 25.

Shoaib and Patten reported 100 women with silicone breast implants from which 84 patients underwent a Magnetic resonance imaging (MRI) of the brain4. Nineteen of these 84 women, of whom nine were clinically diagnosed with multiple sclerosis-like syndrome or brains disease, showed multiple white matter lesions and thirteen women showed multiple small ischemic lesions. At present, it is unknown whether BII patients have altered fMRI scans as well.

Study objective

The aim of this pilot study is to explore the structure and function of brain regions associated with the pain matrix in Breast Implant Illness (BII). This pilot study will be the foundation for grant application for future research.

Study design

This study will be an exploratory pilot functional MRI study to generate a proof-of-evidence that substantiates an idea and increases the likelihood of further grant funding for follow-up research. Therefore, we want to examine 24 women diagnosed with Breast Implant Illness, of which 12 women with breast implants (group 1) and 12 women who already had their implant removed (group 2), and a group of 12 healthy controles with silicone breast implants (group 3) by means of a functional MRI scan with the same protocol, to investigate

functional or structural differences between the groups.

Study burden and risks

No major or minor risks are known to be associated with this study. Subjects can experience the MRI scan as uncomfortable. The scan will take about 45 minutes. Furthermore patients are being asked several questions and an MMSE is conducted. This is no difficult test.

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

Age: 18 to 76 years old

Diagnosis of ASIA-syndrome
No diagnosis of a chronic pain syndrome, fibromyalgia (FM) or chronic fatigue syndrome (CFS).
Silicone filled breast implants (group 1) explanted (group 2)
Cosmetic purpose of silicone breast implants
Cognitive impairment and/or memory disturbances
Competent patients

Controles:
Age: 18 to 76 years old
Matched for implant duration
Healthy (no diagnosis of ASIA-syndrome, a chronic pain syndrome, fibromyalgia (FM) or chronic fatigue syndrome (CFS)).
Silicone filled breast implants
Cosmetic purpose of silicone breast implants
No complaints of cognitive impairment and/or memory disturbances
Competent patients

Exclusion criteria

Cancer
Diabetes Mellitus
Claustrophobia or fear of being in a closed space
Medication (>6 months): antidepressants, any analgesics, anticonvulsants, benzodiazepines
MRI incompatible health condition (i.e., ICD,pacemaker or other metal prosthetic implants)
History of CVA/TIA

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	12-08-2020
Enrollment:	36
Type:	Actual

Ethics review

Approved WMO Date:	21-04-2020
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	16-04-2021
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	27-07-2021
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	23-12-2021
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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	NL72417.068.19