Brain and brainstem activation following duodenal nociceptive stimulation with capsaicin, an exploratory high-resolution fMRI study in healthy volunteers.

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To explore regions of brain and brainstem activation in healthy volunteers during abdominal pain or discomfort after chemical nociceptive stimulation of the duodenum with capsaicin. In the future, we aim to perform the same study in IBS-/FD-patients...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Gastrointestinal motility and defaecation conditions
Study type	Observational invasive

Summary

ID

NL-OMON47774

Source
ToetsingOnline

Brief title
fMRI and visceral perception

Condition

- Gastrointestinal motility and defaecation conditions
- Anxiety disorders and symptoms

Synonym
Irritable Bowel Syndrome (IBS)

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Capsaicin, Functional Gastrointestinal Disorders, Functional Magnetic Resonance, Irritable Bowel Syndrome

Outcome measures

Primary outcome

(ASL-) Voxel-wise blood oxygenation level dependent (BOLD) signal activity in

the NTS.

Secondary outcome

* Voxel-wise blood oxygenation level dependent BOLD signal activity in the

Cingulate Cortex, Insula, Thalamus, Prefrontal Cortex, Primary and Secondary

Somatosensory Cortex, Amygdala, PAG

* Baseline Cerebral Blood Flow

* Visual Analogue Scores during capsaicin and placebo infusion into the duodenum

* Gastro-intestinal Symptom Scores, Depression and Anxiety symptom scores

(HADS, PHQ-9, GAD-7), personality trait (BIG-FIVE-Inventory), Traumata in early

life, quality of life scores (SF-36), current affect scores (PANAS-SF), current

pain scores (BPI-SF) and gastrointestinal symptom scores (GSRS-IBS+), visceral

sensitivity index (VSI)

Study description

Background summary

Brain imaging has shown abnormal brain activations in response to visceral stimulation in patients with the Irritable Bowel Syndrome (IBS). To investigate the possible role of the Nucleus of the Solitary Tract (NTS), the primary relay station in the brainstem for vagal afferents, its activation in IBS and functional dyspepsia patients will be evaluated. Prior to this, an exploratory study in healthy volunteers will be conducted (described in this protocol). This will be the first high magnetic field fMRI study evaluating the possible role of NTS activation in visceral abdominal pain. Moreover, this will be the first fMRI study using duodenal capsaicin infusion as a stimulus, which is more physiological than mechano-stimulation.

Study objective

To explore regions of brain and brainstem activation in healthy volunteers during abdominal pain or discomfort after chemical nociceptive stimulation of the duodenum with capsaicin. In the future, we aim to perform the same study in IBS-/FD-patients to assess differences in fMRI findings related to nociceptive processing and to assess patient characteristics associated with these differences.

Study design

An explorative 7T fMRI study

Intervention

Duodenal capsaicin and placebo (saline + small amount of ethanol) infusion via a nasoduodenal tube.

Study burden and risks

Volunteers will not benefit from participating in this study. There are no risks associated with the introduction of a naso-duodenal tube under fluoroscopy control, the radiation exposure of fluoroscopy is minimal: 0.05mSv. Capsaicin infusion may cause abdominal cramps, a burning sensation, abdominal pain, nausea or heartburn but symptoms will subside rapidly after discontinuation of the infusion. The nasoduodenal tube and infusion pump are safe to use in the magnetic field and have been tested for this purpose extensively. Ultra high magnetic field MRI is very safe and no adverse events are anticipated when taking into account all contra-indications. Solely *Certified Users* will operate the MRI according to approved guidelines and protocol. Subjects will be screened for contraindications (metal implants etc.) prior to inclusion and again on the day of scanning. Some participants may experience mild vertigo, nausea or a metal taste when entering the MRI environment. In extremely rare cases, a small burn may arise due to heating caused by radiofrequency. All participants will be informed about any

unexpected medical findings (MRI findings). In case the subject does not wish to be informed, he is not allowed to participate in this study. Completing questionnaires is non-invasive. Subjects will be informed about the risks and burdens of the measurements beforehand.

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

* Of female sex;
* Based on medical history and previous examination, no gastrointestinal complaints can be defined;
* Age between 18 and 65 years;
* BMI between 18 and 30 kg/m2;
* Women in fertile age (<55 years old) must use contraception or be

postmenopausal for at least two years;
* All subjects should be right-handed.

Exclusion criteria

* Presence of metallic prostheses, pacemakers, metal clips on blood vessels, metal parts in the eye, an intrauterine device, metal braces, facial tattoos (including permanent eye make-up) and/or other metal objects;
* History of major head trauma or head/brain surgery;
* History of claustrophobia;
* History of severe or chronic cardiovascular, respiratory, urogenital, gastrointestinal/ hepatic, hematological/immunologic, HEENT (head, ears, eyes, nose, throat), dermatological/connective tissue, musculoskeletal, metabolic/nutritional, endocrine, neurological/psychiatric diseases, allergy, major surgery and/or laboratory assessments which might limit participation in or completion of the study protocol;
* Use of medication, including vitamin and iron supplementation, except oral contraceptives, within 14 days prior to start of the study;
* Major abdominal surgery interfering with gastrointestinal function (uncomplicated appendectomy, cholecystectomy and hysterectomy allowed, and other surgery upon judgment of the principle investigator);
* Pregnancy, lactation, wish to become pregnant;
* High alcohol consumption (>15 alcoholic consumptions per week);
* Using drugs of abuse;
* Self-admitted HIV-positive state;
* Known allergic reaction to capsaicin;
* High intake of spicy (capsaicin containing) food (meaning an estimated intake of > than 1.5mg/day), due to possible desensitization of the capsaicin receptor TRPV1 (see further below);
* Administration of investigational drugs or participation in any scientific intervention study which may interfere with this study (to be decided by the principle investigator), in the 180 days prior to the study;
* Any evidence of structural brain abnormalities examined by anatomical MRI will lead to exclusion.

Study design

Design

Study type: Observational invasive
Masking: Open (masking not used)

Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	02-11-2016
Enrollment:	26
Type:	Actual

Ethics review

Approved WMO

Date:	15-12-2015
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO

Date:	30-10-2018
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO

Date:	11-07-2019
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
ClinicalTrials.gov	NCT02551029
CCMO	NL51770.068.15