Gut-brain-axis alterations after vagus nerve stimulation in refractory epilepsy

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Seizures (incl subtypes)
Study type	Observational invasive

Summary

ID

NL-OMON51448

Source
ToetsingOnline

Brief title
E-GUT-VNS

Condition

- Seizures (incl subtypes)

Synonym
Refractory epilepsy

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: LivaNova Investigator Initiated Research Grant

Intervention

Keyword: Gut-brain axis, Refractory epilepsy, Vagus nerve stimulation

Outcome measures

Primary outcome

Intestinal permeability (LPS binding protein, main study parameter)

Secondary outcome

Intestinal microbiome, intestinal inflammation (calprotectin), immunological parameters (general immunological function (IL-1-beta, IL-6, IL-8, IL-10, IFN-gamma, TNF-alpha, IL-1RA, CRP); blood-brain-barrier (GFAP, S100b); neurotrophins (neurotrophin-3, BDNF, neurofilament H, neurofilament L); and metabolic factors (IGF-1, IGF-1R, leptin, insulin)), volatile organic compounds (VOC) before and after implantation

Study description

Background summary

Based on the evidence regarding intestinal permeability and microbiome disturbances in patients with epilepsy and in mood disorders, combined with the restoring effects of vagus nerve stimulation (VNS) on intestinal mucosa in animal models and patients with inflammatory bowel disease, we hypothesize that VNS also has an indirect effect on quality-of-life/depressive symptoms/seizure frequency via improvement of microbiota balance, intestinal permeability and an associated decrease in immunological dysregulation in patients with drug resistant epilepsy (DRE).
Furthermore, we hypothesize that in DRE-cases with increased intestinal permeability, intestinal microbiota disbalance and/or immunological aberrations at baseline, VNS will have a stronger ameliorating effect on quality-of-life/depressive symptoms/seizure frequency. These biomarkers may therefore be suitable as potential treatment response predictor candidates.

Study objective

Therefore, this study aims to improve the understanding of the physiological effect of VNS on intestinal permeability, intestinal microbiota, immunological parameters in blood and breath in drug resistant epilepsy (DRE) patients. Additionally, this study aims to predict improvement of quality of life, reduction of depressive symptomatology and seizure frequency one year after VNS implantation, based on these measurements at baseline.

Study design

Observational before and after design.
Measurements will be made before and up to 1 year after clinical VNS implantation. Blood samples, fecal samples, breath samples, epilepsy characteristics and psychometrics (including depression symptomatology), will be taken at baseline, before VNS implantation. These measurements will be repeated 1 year post implantation. Quality of life, depression symptomatology, and epilepsy characteristics will be measured every 3 months in between as well.

Study burden and risks

The number of patient visits will be limited and mainly requires time investment for few physical examinations and questionnaires. Stool samples are collected twice in a developed way that is generally well accepted. Blood samples and breath samples will be collected at two occasions by experienced researchers or lab technicians, so health risk attributable to this procedure is minimal as well.
Potential benefits of participation concern that routine care consists of less extensive monitoring of symptom change and functioning compared to the current trial, so all patients may benefit from the thorough examinations during study participation.
In the face of the limited additional burden for the patient when participating in the current trial as compared to routine treatment, and the possible positive outcome for future treatment, offering participation to selected patients appears to be justified.

Contacts

Public
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9700RB
NL
Scientific

Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9700RB
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Drug-resistent epilepsy (DRE) patients that are accepted for VNS therapy
- Adult (18 years or older) and is capable of providing informed consent

Exclusion criteria

- Pregnancy or breastfeeding (assessed through anamnesis)
- Mental retardation (IQ score <60)
- Any clinically significant or unstable medical disorder as determined by the investigators, including inflammatory bowel disease, short-bowel syndrome or acute/chronic pancreatitis

Study design

Design

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

Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	18-09-2023
Enrollment:	50
Type:	Actual

Ethics review

Approved WMO Date:	29-12-2022
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	14-10-2024
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NL82125.042.22