Clinical Efficacy of Transcutaneous Auricular Vagal Nerve Stimulation in Irritable Bowel Syndrome and the potential predictive role for the Vagal-Autonomic Neurosignature

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Primary objective: To study the clinical efficacy of tVNS for the improvement of abdominal pain in patients with IBS, as measured by the responder rates based on IBS symptom severity score (IBS-SSS) over an 8-week time period. Secondary objectives:...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Gastrointestinal signs and symptoms
Study type	Interventional

Summary

ID

NL-OMON56386

Source
ToetsingOnline

Brief title
RESILIENCE

Condition

- Gastrointestinal signs and symptoms

Synonym
IBS, irritable bowel syndroom

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Maastricht
Source(s) of monetary or material Support: ERC grant

Intervention

Keyword: fMRI, IBS (irritable bowel syndrome), tVNS (transcutenous vagal nerve stimulation), visceral pain

Outcome measures

Primary outcome

A clinically meaningful decrease in severity of GI-symptoms after the 8-week

treatment period, measured using the IBS-SSS defined as a decrease of >= 50

points.

Secondary outcome

- The relation between brain activation profiles including patterns predicted

by the ESM tool in combination with the wearable.

- The value of the multimodal neuro-signature in the prediction of clinical

response to tVNS in IBS-patients.

- Number and severity of adverse events

- Symptoms of anxiety and depression

- Direct and indirect costs made during the treatment period

- Satisfaction with the treatment

- The amount of time patients used the tVNS device

- The comparison of microbiota before and after treatmen

Study description

Background summary

The prevalence of irritable bowel syndrome (IBS) in the general population is 5%. IBS affects all age groups across the life span, generally appearing in late adolescence/early adulthood. Despite the known prevalence and impact of IBS, its pathophysiology remains unclear. Current consensus, as per the Rome IV criteria, considers IBS a disorder of the gut-brain interaction, reflecting the unique bidirectional communication between these two organ systems. In this study we aim to study the efficacy of a new treatment strategy, namely transcutaneous auricular vagus nerve stimulation (tVNS). tVNS consisting of small electrodes that interface with the concha of the outer ear. This area corresponds to the only place on the surface of the human body where there is afferent vagal innervation. tVNS is safe, well-tolerated and user-friendly. Studies have pointed towards beneficial effects of tVNS in depression, epilepsy and tinnitus, among others, but firmly establishing its therapeutic efficacy remains warranted. In addition, mechanistic evidence supporting the therapeutic potential of tVNS is still lacking. Therefore, tVNS is not yet ready for application in routine clinical practice for any of these conditions. Restoring the sympathico-vagal disbalance through tVNS can perhaps decrease sensitivity to pain in IBS. With this study, new results of this potential novel therapeutic target could fundamentally change the therapeutic landscape of IBS and other pain disorders.

Study objective

Primary objective: To study the clinical efficacy of tVNS for the improvement of abdominal pain in patients with IBS, as measured by the responder rates based on IBS symptom severity score (IBS-SSS) over an 8-week time period.

Secondary objectives:
To ascertain whether the autonomic-vagal neurosignature, derived from pre-treatment registration of symptom profiles, autonomic responses and imaging of neuronal activity as a reaction to stress is able to accurately predict therapeutic response to tVNS.
To evaluate the effect of treatment on quality of life
To evaluate the effect of treatment on depression
To evaluate the effect of treatment on anxiety
To evaluate the effect of treatment on microbiota composition

Study design

This is a single centre, prospective, randomized, double-blind, two-group (1:1) parallel intervention study for 9 weeks with 6 month follow up.

Intervention

Group 1 will receive tVNS treatment during 8 weeks, group 2 will be a sham group with a non-conducting electrode.

Study burden and risks

This study does not involve any incapacitated or minority groups and is considered a low-risk study. The patients in the comparator group will continue with their treatment as usual, without receiving any additional treatment. As such, this group of patients is not expected to benefit directly from participation during the treatment period. Patients in the intervention group are expected to benefit from the treatment in terms of a reduction of IBS complaints. Serious adverse events have not been reported in studies examining the efficacy of the tVNS device. Subjects need to visit the university three times. In the first week they need to complete the ESM and use the Fitbit during their daily life. During the tVNS treatment, they need to fill in an electronic questionnaire once a week. Participants will be asked to fill in electronic questionnaires again after 3 and 6 months after completing the tVNS treatment.

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

- Patients with IBS according to Rome IV criteria
- Aged between 18-75 years
- Ability to understand and speak the Dutch language.
- Ability to understand how to utilize the ESM application.

Exclusion criteria

- Any organic explanation for the abdominal symptoms;
- A history of abdominal surgery, except for uncomplicated appendectomy, laparoscopic cholecystectomy and hysterectomy is present or otherwise based on the principal investigator*s judgement.
- Presence of metallic prostheses, pacemakers, metal clips on blood vessels, metal parts in the eye, an intrauterine device (with the exception of the Mirena IUD), metal braces, facial tattoos and/or metal objects.
- History of major head trauma or head/brain surgery
- History of claustrophobia
- Pregnancy, lactation, intention to become pregnant during the study period

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	20-02-2024
Enrollment:	166
Type:	Actual

Medical products/devices used

Generic name:	tVNS (transcutaneous vagal nerve stimulator)
Registration:	Yes - CE outside intended use

Ethics review

Approved WMO Date:	29-09-2023
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	06-02-2024
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	26-08-2024
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	NL84720.068.23