Exploring the effect of Transcutaneous Auricular Vagus Nerve Stimulation (taVNS) on the acute stress responses.

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Ethical review	Approved WMO
Status	Pending
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON57099

Source
ToetsingOnline

Brief title
tVNS and autonomic responses.

Condition

- Other condition

Synonym
Healthy individuals

Health condition

Gezonde proefpersonen

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Acute stress response, MAST (Maastricht Acute Stress Task), tVNS (transcutaneous Vagus Nerve Stimulation), Vagus nerve

Outcome measures

Primary outcome

The primary endpoint is a significant reduction in the neuroendocrine stress response, measured by saliva cortisol samples, in the taVNS group compared to the sham treatment group following the MAST.

Secondary outcome

Secondary endpoints are:

- Subjective stress responses to the MAST following taVNS or sham treatment, assessed through scores on the I-PANAS-SF and 0-100 Visual Analog Scales (VAS);

- Autonomic response to stress following taVNS or sham treatment and the MAST, assessed using a combination of blood pressure monitoring, Fitbit smartwatch, and the Shimmer3 GSR sensor;

- Stress responses in relation to potential affective symptoms and personality traits, using the GAD-7, PHQ-9, and BFI;

- Number and severity of adverse events.

Study description

Background summary

Dysregulation of the autonomic nervous system (ANS) has been shown to be associated with various diseases. Stress is a significant factor capable of inducing such sympatico-vagal imbalance by favouring sympathetic responses. Restoring normal vagal tone is a key objective in treating these conditions. Transcutaneous auricular vagus nerve stimulation (taVNS) offers a non-invasive approach to modulate the ANS, given the unique access point of the external ear to the vagus nerve. This modulation can influence numerous physiological processes and bodily states associated with information transfer between the brain and the body. While previous studies show promising results, the precise physiological impact of taVNS on vagal or autonomic function remains unclear. A better understanding of the mechanisms of action for taVNS is essential for implementing taVNS-based treatment strategies in everyday practice.

Study objective

The primary aim of this study is to assess the efficacy of taVNS in mitigating the acute stress response induced by the Maastricht Acute Stress Task (MAST) among healthy subjects, measured by cortisol levels in saliva samples.

Secondary objectives include:
- Evaluating taVNS*s potential to counteract stress-induced sympathetic activation and thereby alleviate stress-related effects, including negative affect, as measuring using the I-PANAS-SF questionnaire, and feelings of stress, pain, and unpleasantness, as measured with 0-100 Visual Analog Scales (VAS)
- Assessing its impact on autonomic outflow parameters, , using a blood pressure monitor for blood pressure, and a FitBit smartwatch for heart rate variability, and Shimmer3 GSR sensor for heart rate variability and skin conductance. .
- Evaluating the relationship between stress responses and affective symptoms and personality traits, utilizing the Generalized Anxiety Disorder 7-Item Scale (GAD-7), Patient Health Questionnaire (PHQ-9), and the Big Five Inventory (BFI).

Study design

This study concerns a single-centre, prospective, double-blind, randomized, placebo-controlled interventional trial with a (1:1) parallel design, with all measurements conducted at Maastricht University.

Intervention

Participants will be randomly assigned to either the taVNS or sham stimulation group, administered 30 minutes before the MAST.

Study burden and risks

This study, involving 60 healthy volunteers aged 18-65 years, is a low-risk interventional study. Participants will undergo two short visits: an initial visit for obtaining written informed consent and completing (digital) questionnaires, and a test day lasting 2-3 hours. During the test day, participants will receive either 30 minutes of taVNS or sham stimulation, followed by the 15-minute MAST. Participants will rate feelings of negative affect using the I-PANAS-SF and assess their perceived stress, pain, and unpleasantness using 0-100 Visual Analogue Scales (VASs)/ Saliva cortisol samples will be taken at eight fixed time points, up to 55 minutes after the MAST. The study does not involve incapacitated or minority groups. While participants will not directly benefit, risks are minor and proportional to scientific value. TaVNS is non-invasive, with no reported serious adverse events. The MAST is a well-established research tool and is not expected to induce negative effects beyond mild discomfort and emotional responses. Additional procedures include administering questionnaires, collecting cortisol saliva samples, and measuring autonomic parameters. All these procedures carry minimal risks.

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

- Healthy participants (defined as those without a pre-existing medical comorbidity)
- Aged between 18-65 years
- Ability to understand and speak the Dutch language.

Exclusion criteria

- Medical history or condition affecting the cardiovascular, respiratory, urogenital, gastrointestinal/hepatic, haematologic/immunologic, HEENT (head, ears, eyes, nose, throat), dermatological/connective tissue, musculoskeletal, metabolic/nutritional, endocrine, neurological/psychiatric systems, as well as prior major surgeries or ongoing laboratory abnormalities that could potentially limit participation or completion of the study protocol;
- Any use of medication, especially those that may influence the autonomic nervous system or the hypothalamus-pituitary-adrenal axis (e.g., beta-agonists or corticosteroids), with the exception of contraceptives and paracetamol;
- Current or lifetime psychopathology (including PHQ-9 and GHD-7 scores > 10);
- Substance abuse (including excessive alcohol consumption);
- Smoking;
- Pregnancy, lactation, or intention to become pregnant during the study period;
- Use of devices (e.g., cochlear implants) or other reasons (e.g. wounds, permanent ear-piercing) which complicate the use of the tVNS device;
- Participation in another clinical study in which the MAST was used;
- Administration of investigational drugs or participation in any scientific intervention study that might interfere with this study (to be determined by the principal investigator) within 180 days preceding the commencement of the study;
- Students and employees of Maastricht University are not precluded from participation, unless they have a direct personal, professional or hierarchical position with regards to any of the study team members or their department.

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:	Pending
Start date (anticipated):	01-02-2025
Enrollment:	60
Type:	Anticipated

Medical products/devices used

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

Ethics review

Approved WMO Date:	26-08-2024
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	06-03-2025
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	NL87188.068.24