Auricular vagal nerve stimulation combined with rehabilitation to enhance functional outcome in cerebral palsy patients with upper extremity deficits (AVANS study) Part1

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Ethical review	Approved WMO
Status	Pending
Health condition type	Structural brain disorders
Study type	Interventional

Summary

ID

NL-OMON57283

Source
ToetsingOnline

Brief title
AVANS

Condition

- Structural brain disorders

Synonym
cerebral palsy, spasticity

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: auriculair vagal nerve stimulation, cerebral palsy, neuromodulation, stroke

Outcome measures

Primary outcome

Motor Evoked Potential (MEP) parameters will be assessed before and after the

task to measure changes in cortical plasticity.

Secondary outcome

The secondary outcome parameters are the difference in motor performance during

the stacking test and the difference in somatosensory evoked potential (SSEP),

different stimulation intensities will be tested.

Study description

Background summary

Most children with Cerebral Palsy (CP) experience impaired hand function, resulting in difficulties performing daily activities. Intensive physical rehabilitation programs, using variants of bimanual training (BIMT) or constraint-induced movement therapy (CIMT), positively affect functional outcomes and have been shown to result in beneficial structural neuroplastic changes including the reorganization of the sensorimotor network. Such neuroplastic changes may also be induced by means of neuromodulation technologies. Functional outcomes could therefore be enhanced by combining physical rehabilitation with concomitant non-invasive neuromodulation. Non-invasive auricular vagal nerve stimulation (aVNS) is already used in this way with promising results for rehabilitation of adult stroke patients. In these studies the focus was functional improvement after the training program, none of these studies focused on the underlying neuroplastic changes. To this date, no studies have investigated the use in children suffering from CP. However, before testing such a combination therapy in children, further

research into mechanisms underlying neuroplastic changes is necessary.

Study objective

The ultimate goal is to investigate whether aVNS can enhance cortical plasticity and improve functional outcomes during intensive rehabilitation programs in children with cerebral palsy. First, we aim to establish the extent of cortical plasticity changes after aVNS in healthy adult volunteers (part 1). Secondly, we aim to establish the proof of principle in combining aVNS and rehabilitation for enhanced functional outcomes in adult stroke patients (part 2) and in children with cerebral palsy (part 3); a separate research proposal will be submitted. We hypothesize that medium-intensity aVNS induces cortical plasticity and enhances functional recovery.

Study design

Randomized controlled trial

Intervention

It is unknown which aVNS stimulation intensity is the most effective in inducing cortical plasticity and improving the performance of a simple motor task. Therefore, the group will be divided into three subgroups, testing different stimulation intensities both during a simple motor task and at rest. To account for individual differences in the primary outcome measure, i.e. motor evoked potential (MEP), each participant will act as their own control and will receive both sham and stimulation, with and without a motor task at the allocated intensity during four visits. The order of the tested conditions will be randomized. The aVNS stimulation (sham/stimulation) will last 30 minutes.

Study burden and risks

Part 1: the sham-controlled study in healthy adult volunteers will consist of four visits. During these visits, first MEP, SSEP and stacking test are performed, followed by one of the conditions below:
30 min sham stimulation during rest
30 min sham stimulation during performance of a simple motor task
30 min aVNS stimulation at the allocated intensity during rest
30 min aVNS stimulation at the allocated intensity during performance of a simple motor task
At each visit a repeated MEP, SSEP and stacking test are performed pre and post aVNS stimulation/sham. We ask the participants not to practice between the visits, they will not be required to perform other tasks.
A literature search of side effects of aVNS showed no severe adverse events during the treatment of children with epilepsy. Among 229 adult stroke patients

using aVNS, only one patient with a local skin reaction(redness) was reported.
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Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Healthy subjects aged 18-70 years
Proficient in Dutch language
Sufficient cognitive function to follow instructions

Exclusion criteria

History of stroke/ epilepsy or other neurological impairments

Functional impairments/ pain/ sensory deficits of hand/arm.
Previous injury or intervention of the vagal nerve
Persons with cardiac diseases

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):	01-10-2024
Enrollment:	36
Type:	Anticipated

Medical products/devices used

Generic name:	auricular vagal nerve stimulation
Registration:	Yes - CE intended use

Ethics review

Approved WMO

Date:	03-02-2025
Application type:	First submission
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	NL86700.068.24