THE EFFECT OF VAGUS NERVE STIMULATION ON PRO-AND ANTI-INFLAMMATORY CYTOKINES IN PATIENTS WITH REFRACTORY EPILEPSY

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1) To study the effect of VNS on the aberrant set point of the monocyte-macrophage-dendritic cell system in patients with refractory epilepsy 2) To investigate whether a correction of this setpoint induces anticonvulsive and neuroprotective effects...

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

Summary

ID

NL-OMON29828

Source
ToetsingOnline

Brief title
VNmood

Condition

- Seizures (incl subtypes)

Synonym
Epilepsy

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Ziekenhuis Maastricht

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Epilepsy, Nerve, Stimulation, Vagus

Outcome measures

Primary outcome

> 50% seizure reduction

Secondary outcome

Demographic data and epilepsy specific data:

- age

- gender

- seizure and epilepsy syndrome classification

- duration of epilepsy

- seizure frequency (diary)

- seizure severity

Neuro-immunologic variables (pro-, and anti-inflammatory cytokines and

neuroprotective cytokines)

Biochemical variables (serotonin metabolites, GABA, glutamate)

Endocrine variables (cortisol)

Neuropsychologic variables (mood and quality of life)

Study description

Background summary

Repetitive seizures increase pro*inflammatory cytokines in the peripheral blood. Experimentally it has been shown that activation of inflammatory

cytokines by peripheral administration of a toxic agens causes sickness behaviour. Pro-inflammatory cytokines interfere with the catabolisation of a precursor of Serotonin (Tryptophan). Tryptophan is catabolised to an endogen NMDA receptor agonist. NMDA (an excitatory neurotransmitter) produce neuronal damage.
The Vagus Nerve (VN) plays an important role in the interaction between the immune and neurotransmitter system in which cytokines are crucial. Vagus nerve stimulation (VNS) is associated with marked peripheral increases in pro-, and anti-inflammatory cytokines. VNS has also an effect on various amino-acid pools in the brain. Given the complexity of the immune system and its interaction with neurotransmitter and endocrine systems in the human brain it is not surprising to find that pro-,and anti-inflammatory immune factors play a role in the etiology and the course of affective disorders. It is to be expected that immune modulation also plays a role in the course of epilepsy.

Study objective

1) To study the effect of VNS on the aberrant set point of the monocyte-macrophage-dendritic cell system in patients with refractory epilepsy
2) To investigate whether a correction of this setpoint induces anticonvulsive and neuroprotective effects

Study design

Study design: Prospective observational longitudinal cohort.

The VNS device is implanted after a baseline period of three month. Two weeks after surgery activation of the device will take place.
At the baseline, two weeks after surgery and after six month of actual treatment neurocognitive screening and blood analysis will take place. During the total study period the patients will list their seizures using a seizure diary.

Study burden and risks

Patients who participate in the VN Mood study will have four extra bloodsamplings and two neuropsychologic screening sessions. On two occasions bloodsampling will include a dexamethason test (1 mg dexamethason taken on the evening prior to bloodsampling). There are no risk factors other than the risk factors seen in usual VNS treatment. The benefit for the individual patient: the extra information on mood, and quality of life as well as the information on several biochemical and pharmacologic parameters may be of help in guiding the patient.

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

1) Patients treated with Vagus Nerve stimulation as part of usual patient care
2) Age 18 years or older
3) Informed consent

Exclusion criteria

1) Evidence of a progressive cerebral lesion, degenerative disorder, malignancy or a history with malignancy in the past 5 years
2) Unstable medical disease (i.e. cardiovascular, hepatic, renal, gynaecologic, musculoskeletal, gastrointestinal, metabolic, endocrine) in the last 2 years
3) Documented history with generalized status epilepticus in the past three months

4) High risks for complications (obstructive respiratory disease, gastric disorders, cardiac rythm disorders)
5) A history of alcohol or drug abuse, of psychiatric disorder requiring electro-convulsive therapy, chronic use of major tranquillisers (neuroleptics, antidepressants, or MAO inhibitors) in the past 6 months
6) Regularly treatment with antihistamines, metoclopramide or CNS-active compounds
7) Treatment with an experimental drug during the past 30 days
8) Subjects who are schizophrenic or have exhibited any psychotic symptomatology

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	15-10-2006
Enrollment:	30
Type:	Actual

Ethics review

Approved WMO

Date:	06-09-2006
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	NL13166.068.06