REstoring CONsciousness with NEurostimulation of the Central Thalamus in patients with a persistent minimally conscious state (RECONNECT): a pilot study

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To explore the efficacy of central thalamic DBS in restoring consciousness in MCS patients. Hypothesis: Central thalamic DBS improves the level of consciousness in MCS patients.

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

Summary

ID

NL-OMON54701

Source
ToetsingOnline

Brief title
RECONNECT

Condition

- Other condition
- Structural brain disorders

Synonym
Minimally conscious state, minimally responsive state

Health condition

chronische bewustzijnsstoornissen

Research involving
Human

Sponsors and support

Primary sponsor: Amsterdam UMC
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Brain injury, Deep brain stimulation, Disorders of consciousness, Minimally conscious state

Outcome measures

Primary outcome

The primary outcome of this study is the change on the CRS-R and the number of patients that emerges from MCS.

Secondary outcome

Secondary endpoints are changes on a subset of additional behavioral scales for patients recovering from coma (PALOC-S, DRS), the effects of DBS treatment on the perceived change of consciousness and its appreciation by family members, and the quality of life and health in family members as measured by the WHOQOL-BREF. Moreover, neurophysiological parameters will be compared between the preoperative and postoperatieve state using MEG.

Study description

Background summary

The unresponsive wakefulness syndrome (UWS) and minimally conscious state (MCS) are disorders of consciousness that are among the most dramatic conditions in medicine. There is currently no treatment for improvement or restoration of the level of consciousness. It is hypothesized that chronic hypo-activation of central thalamic outflow tracts to the cortex is the main cause of disorders of

consciousness. While UWS patients only have periods of wakefulness, MCS patients show partial preservation of conscious awareness. Moreover, recent neuroimaging studies in MCS patients show sparing of cortical connectivity, which provides the necessary substrate to harness the effects of explorative interventions to restore consciousness. Since the 1960s, deep brain stimulation (DBS) of the central thalamus has been applied in small, uncontrolled patient series, mostly consisting of UWS patients. Behavioral responsiveness was reported in many cases, especially in MCS patients, but methodological weaknesses, such as inclusion within the known time-frame of natural recovery makes it impossible to judge whether the improvements were due to the DBS itself. A clinical DBS trial with a series of persistent MCS patients has not been performed, but is much awaited by the international community.

Study objective

To explore the efficacy of central thalamic DBS in restoring consciousness in MCS patients.

Hypothesis: Central thalamic DBS improves the level of consciousness in MCS patients.

Study design

A prospective pilot study.

Intervention

DBS electrodes will be implanted bilaterally in the central thalamus and connected to a pulse generator that is placed under the skin of the chest.

Study burden and risks

There is currently no evidence-based treatment for improvement or restoration of consciousness in patients suffering from persistent MCS. A large group of (relatively young) patients ends up in nursing homes without perspective. DBS is accepted as a safe, adjustable and reversible neurosurgical technique to modulate brain functioning, and its application in various neurologic and neuropsychiatric disorders is steadily expanding. Participation in the RECONNECT pilot study requires a short hospital admission, DBS surgery, and serial follow-up with four behavioral assessments. Also, two non-invasive MEG-scans will be made (in the VUmc). Despite the burden of the RECONNECT pilot study, it provides an opportunity to restore consciousness and perhaps some of the decision-making capacity of participating patients. The RECONNECT study is directed to improve care for patients with disorders of consciousness and will contribute to further development of scientific foundations of electrical stimulation of the brain network that regulates consciousness. Therefore, it

might benefit a much larger group of patients with severe brain damage and (chronic) disorders of consciousness. Finally, the results of this pilot-study may define a rationale for further research and contribute to the determination of criteria for selection of patients eligible for DBS. If results of this pilot-study are positive, and the analysis shows that DBS has a significant impact on both arousal and behavioral awareness, a larger randomized, double-blind, clinical cross-over study will be proposed.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

• Age 18-65 years
• Diagnosis of MCS according to CRS-R
• The patient is in persistent MCS, i.e. at least 24 months post-injury
• MCS is caused by non-progressive traumatic brain injury (TBI)

• MCS is treatment-refractory, defined as:
- not accompanied by concomitant hydrocephalus
or
- accompanied by concomitant hydrocephalus that has been adequately treated by permanent cerebrospinal fluid shunting for at least six months with no evidence of improvement in neurobehavioral function in the last two months prior to enrolment
and
- previous failure of emergence from MCS by treatment with amantadine, levodopa and zolpidem
• Independent ventilation
• Stable physical condition
• Written informed consent by primary family caregivers

Exclusion criteria

• Expectation that patients will not be able to meaningfully interact with the outside world even when consciousness is restored, defined as:
- evidence of significant lesions involving cortical language areas (Wernicke's and/or Broca's - area) or brainstem on MRI
or
- quadriplegia due to spinal cord injury, brainstem injury, or bilateral loss of motor cortex on MRI
• Premorbid mental retardation
• MRI-incompatible cardiac pacemaker/defibrillator
• Intractable seizure disorders (status epilepticus)
• Presence of untreated endocrine disturbances (i.e., hyper- or hypothyroidism) or other biochemical disturbances
• Medical contraindications for DBS or general anesthesia, and comorbid conditions, including:
- non-closed skull due to previous decompressive hemicraniectomy without proper cranioplasty
- anatomical barriers for electrode placement on MRI
- local, systemic, acute, or chronic infectious illness
- severe collagen vascular disorder/bleeding disorders
- severe chronic pulmonary disease
- life-threatening cardiac arrhythmias
- kidney failure or other major organ systems failures
- other active neurologic diseases/processes (i.e., multiple sclerosis, Parkinson*s disease, Alzheimer*s disease)
- neoplasm with life expectancy <5 years

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	28-10-2019
Enrollment:	6
Type:	Actual

Medical products/devices used

Generic name:	Deep brain stimulation (DBS)
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	23-01-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-05-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	NL58841.018.16