Deep Brain Stimulation (DBS) in anorexia nervosa.

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Ethische beoordeling	Positief advies
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON29125

Bron
Nationaal Trial Register

Verkorte titel
DBS-AN

Aandoening

Anorexia nervosa; eating disorders; deep brain stimulation
Anorexia nervosa; eetstoornissen; diepe hersenstimulatie

Ondersteuning

Primaire sponsor: Prof. dr. D.A.J.P. Denys
Academic Medical Centre (AMC), department of psychiatry
Overige ondersteuning: Fonds = verrichter = sponsor

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Treatment effects will be established using within-subject analyses comparing baseline characteristics(T-1) with patient reports during the optimization phase (T1 and T2), and during the maintenance phase (T3 and T4). Primary outcome measurements are:
1. Physical outcome: Weight improvement/BMI;
2. Psychological outcome: Score on the Yale-Brown-Cornell Eating Disorder Scale (YBC- EDS; Mazure e.a. 1994, Dutch translation by our department with back-translation to ensure conceptual equivalence).
3. Quality of life: Score on the EDQOL (Eating Disorders Quality of Life; Engel e.a. 2006).

Toelichting onderzoek

Achtergrond van het onderzoek

Rationale:
Anorexia nervosa (AN) is a severe psychiatric condition with high rates of morbidity, comorbidity and mortality. Many parallels between obsessive-compulsive disorder (OCD) and anorexia nervosa have been drawn with regard to symptomatology and pathophysiology. AN consists of obsessive (weight gain) and compulsive behaviours (dieting, exercising) that, similar to OCD, are related to a dysfunction of the mesolimbic reward system. It is conceivable that the significant relapse and failure rates of

current anorexia nervosa treatments may be at least in part the result of this dysregulated reward system.
We hypothesize that in line with the positive outcome following deep brain stimulation (DBS) in OCD, modulating the reward circuitry in AN may provide 1) significant and sustained improvement in anorexia nervosa symptoms and associated comorbidities and complications and 2) effectively lessen relapse rates associated with the current anorexia treatments.

Objective:
Pilot study to demonstrate the efficacy, feasibility and safety of deep brain stimulation in patients with chronic, treatment-refractory anorexia nervosa. Additionally, the functional effects of deep brain stimulation will be explored by associating the clinical outcome parameters with fMRI, EEG changes, and neuropsychological functioning.

Study design:
Pilot study consisting of treatment with deep brain stimulation targeted at the anterior limb of the capsula interna (ALIC), with an initial 3-9 months optimization phase, followed by a 12 months maintenance phase.

Study population:

Six patients (age range 25-65 years) with chronic treatment refractory anorexia nervosa, defined as meeting the diagnostic criteria for AN continuously in minimally the previous 10 years and not having achieved remission with two or more typical modes of treatment.

Intervention:

Treatment with bilateral deep brain stimulation targeted at the nucleus accumbens with stimulation at the ventral anterior limb of the capsula interna.

Main study parameters/endpoints:

Primary outcome measures are the change in body weight/BMI, score change from baseline on the Yale-Brown-Cornell Eating Disorder Scale (YBC-EDS) and score change from baseline on the Eating Disoder Quality of Life (EDQOL). Secondary outcome measurements include score change from baseline on the Eating Disorder Inventory (EDI-II), the Eating Disorder Examination Questionnaire (EDE-Q), and the Nederlandse Vragenlijst voor Eetgedrag (NVE). Furthermore, functional effects and safety of DBS will be explored by neuroimaging (fMRI), electro-encephalography (EEG) and neuropsychological evaluation.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness:
The greatest burden on the patient during this study is the intervention itself. Potential risks consist of the risks associated with the surgical procedures (i.e. a risk < 1% of intracranial haemorrhage and 3-4% of infection). Patients will be admitted to the hospital during the surgery phase. Changes in somatic condition and potential refeeding syndrome will be monitored closely. At several timepoints patients will be asked to come to the AMC to participate in clinical interviews, questionnaires, neuroimaging, and neuropsychological tests. The neuroimaging and neuropsychological substudies are considered safe in patients with DBS.

Countries of recruitment: The Netherlands.

Doel van het onderzoek

Anorexia Nervosa (AN) is a serious condition and forms a major public health problem. The disorder affects biological, psychological as well as social functioning, affects mainly young people, tends to take on a chronic course in a considerable percentage of patients, has a high mortality rate and although there are many different treatment approaches, up to date, there is no evidence based treatment for AN.

AN is possibly the most homogenous of all psychiatric disorders. There is a narrow age of onset, a stereotypic presentation of symptoms and course, and relative gender specificity. AN patients show similarities with obsessive-compulsive disorder (OCD) patients (Altman e.a. 2009; Kaye e.a. 2006; Godart e.a. 2003; Speranza e.a. 2001). Individuals with AN are preoccupied with food and eating rituals to the point of obsession. They have a distorted body image and compulsively over-exercise. AN patients are characterised by obsessive-compulsive personality traits that manifest predominantly in maladaptive preoccupation with food, weight and body shape. Furthermore, patients with AN have elevated rates of lifetime

diagnoses of comorbid anxiety (obsessive compulsive) and depressive disorders.

Numerous observers have documented the importance of the mesolimbic reward system in the pathophysiology of anorexia nervosa.

Deep Brain Stimulation (DBS) is an innovative and promising approach for the treatment of patients with therapy-refractory reward-related psychiatric disorders (Bewernick e.a. 2010; Denys 2009; Schlaepfer e.a. 2008; Okun e.a. 2007; Greenberg e.a. 2006; Sturm e.a. 2003) by modulating the reward-circuitry in the brain.

The department of psychiatry of the Academical Medical Centre (AMC) Amsterdam is one of the few centers in Europe performing DBS for complex psychiatric disorders. Currently, our center has experience in obsessive-compulsive disorder, addiction and major depressive disorder. In all these disorders, DBS targets reward related brain areas such as the nucleus accumbens and the ventral striatum.

We propose to introduce DBS for anorexia nervosa based on:

1. Our clinical experience with DBS of the NAc region as a safe, reversible and effective treatment for therapy-refractory reward-related psychiatric disorders;

2. The literature on the important role of the reward neurocircuitry in the pathophysiology of anorexia nervosa;

3. The existing knowledge of/experience with animal models of anorexia nervosa and human imaging studies on anorexia nervosa.

We hypothesize that treating treatment refractory

anorexia nervosa patients with DBS in the area of the NAc

and vALIC will result in clinically significant weight

restoration and associated comorbidities and

complications and significant improvement of anorexia

nervosa symptoms reflected by scores on the Yale-Brown-Cornell Eating Disorder Scale (YBC-EDS).

Onderzoeksopzet

T-1:Preoperative phase;

T0: Surgery phase;

T1: Start optimization phase (DBS off);

T2: End optimization phase (DBS on)

T3: Maintenance phase (26 weeks);

T4: End of maintenance phase (52 weeks) = end of study;

Onderzoeksproduct en/of interventie

The intervention of this study will be Deep Brain Stimulation (DBS) in the ventral limb of the capsula interna. Deep Brain stimulation is an adjustable, reversible, non-destructive intervention using a surgically implanted medical device to deliver carefully controlled electrical pulses to precisely targeted areas of the brain. The stimulation can be programmed and adjusted non-invasively by a trained physician to maximize symptom control and minimize side effects. The ventral limb of the capsula interna has been chosen because both animal and human studies indicate that this location is promising for DBS treatment of anorexia nervosa and because this location has shown to be safe in DBS studies among humans with other psychiatric/reward-related disorders such as OCD, depression, and addiction.

Contactpersonen

Publiek

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Primary diagnosis: Anorexia Nervosa (restricting or

purging type; 307.1) according to the DSM-IV criteria

based on a psychiatric interview;

2. Chronicity, defined by an illness duration > 10 years;

3. Disabling severity with substantial functional

impairment according to the DSM-IV criterion C and a

Global Assessment of Function (GAF) score of 45 or less for

at least two years;

4. Treatment refractoriness, defined as lack of response to two or more typical modes of treatment, including one hospital admission or inpatient treatment in a specialized clinic, as described in the Multidisciplinaire Richtlijn Eetstoornissen (Trimbosinstituut 2008);

5. BMI < 15 (level of severity according to the DSM V: extreme);

6. Age: 25-65 years old;

7. Written informed consent;

8Dutch or English speaking and able to answer the study questions;

9.Capable to make his or her own choice without coercion.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Unstable physical condition (severe electrolyte disturbances, cardiac failure, other physical contraindications for surgery/anesthesia, unability to stop the use of anticoagulants;

2. Treatable underlying cause of anorexia/underweight;

3. Active neurological disease like Parkinson’s disease, dementia, epilepsy;

4. Schizophrenia/history of psychosis, bipolar disorder; major depressive disorder;

5. Alcohol or substance abuse (including benzodiazepines)

during the last 6 months;

6. Current Tic disorder;

7. Antisocial personality disorder;

8. Standard MRI scan exclusion criteria (pregnancy,

pacemaker and metals contraindicated for MRI);

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Anders
Toewijzing:	N.v.t. / één studie arm
Blindering:	Dubbelblind
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	01-12-2015
Aantal proefpersonen:	6
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	10-06-2012
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL3322
NTR-old	NTR3469
Ander register	MEC AMC : 40930
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Resultaten

Samenvatting resultaten
N/A