Coherence Analyses in Hyperkinetic Movement Disorders

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1. Investigate whether per-operative subcortico-muscular (LFP-EMG) coherence can be used as a predictor for favourable surgical outcome in DYS and PD tremor patients undergoing DBS surgery 2. Investigate whether pre-surgical EEG-EMG-coherence and...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Movement disorders (incl parkinsonism)
Study type	Observational non invasive

Summary

ID

NL-OMON42214

Source
ToetsingOnline

Brief title
Coherence Analyses HMD

Condition

- Movement disorders (incl parkinsonism)
- Nervous system, skull and spine therapeutic procedures

Synonym
dystonia, essential tremor., Hyperkinetic movement disorders; Parkinson

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Coherence analyses, Deep brain stimulation, Hyperkinetic movement disorders, Neurology / neurosurgery

Outcome measures

Primary outcome

In all patients: Relation between LFP-EMG coherence and clinical effect of DBS quantified by the difference pre- and post-surgery on the specific movement disorder rating scales.

Secondary outcome

In DYS: Cortico-muscular (EEG-EMG), intra-muscular (EMG-EMG) coherence, and *Burke-Fahn-Marsden dystonia rating scale* (BFMDRS) values pre- and post-DBS-surgery.

In PD: Cortico-muscular (EEG-EMG + accelerometer) coherence, intra-muscular (EMG-EMG), and tremor severity assessed with tremor items of the motor (third) part of the unified Parkinson's disease rating scale (UPDRS) values pre- and post-DBS-surgery.

Study description

Background summary

Hyperkinetic neurological movement disorder (HMD) encompass, among others, dystonia, myoclonus and tremor. The exact pathophysiology of most of these abnormal involuntary movements is unknown. Occasionally, HMD is due to lesions in the nervous systems, but usually it is due to functional changes in dysfunctional neural networks including the so called *cortico-basal ganglia thalamo-cortical (CBGTC) loop* (Lehéricy et al., 2013).
To increase our knowledge of the pathophysiology of HMD we will study functional changes in the motor systems in HMD by using analysis techniques, i.e. frequency domain (coherence) and time domain (cumulant density) analyses

of recordings at different levels of the motor pathway.
Coherence is the phase synchrony of two or more signals and can be quantified using the cross-correlation function (Windhorst & Johansson, 1999). To better determine whether signal A causes B in coherent signals or vice versa, additional cumulant density analyses can be performed (Windhorst & Johansson, 1999).
Further understanding of the pathophysiology of HMD could lead to a better application of the current DBS techniques by stimulating where neural activity is most disturbed. Next to this, further understanding of the pathophysiology of HMD could also lead to future, adaptive DBS algorithms (Little et al., 2013), that only stimulate when neural activity is disturbed.
DBS of different basal ganglia targets has proven effective for several movement disorders. The internal part of the globus pallidus (GPi) has become an established treatment for primary generalised dystonia. The same holds for stimulation of the ventral intermediate nucleus (Vim) of the thalamus in ET. PD tremor is treated with either GPi or subthalamic nucleus (STN).
In dystonia, converging evidence shows that excessive oscillatory activity in the brain drives dystonic muscles (Foncke et al., 2007a; Sharott et al., 2008; Tijssen et al., 2000; Tsang et al., 2012). This so called *dystonic drive* was detected in idiopathic dystonia in which 4-7 Hz coherent, phase locked EMG activity was present in cervical musculature (Tijssen et al., 2000). This pathological coherence pattern was also seen between LFP*s of the GPi and dystonic muscles (Foncke et al., 2007a; Sharott et al., 2008). These findings support the disrupted oscillatory activity in the previous mentioned CBGTC loop (Lehéricy et al., 2013). Little data is available on the effect of DBS post-operatively on the intra-muscular dystonic drive and whether DBS electrodes with the highest coherence in these lower 4-7 Hz frequencies are most suitable for (adaptive) stimulation.
In ET, cortico-muscular coherence is also present. The frequency of this coherence is at the tremor frequency of around 6-8 Hz (Hellwig et al., 2001). Similar subcortico-muscular coherence patterns are also present between the VIM and the involved muscles (Pedrosa et al., 2012). However, it is not known whether strong cortico-muscular coherence patterns predict DBS outcome and whether LFP*s with the highest subcortico-muscular coherence are best suitable for (adaptive) stimulation.
PD tremor is typically a resting tremor among 3-7 Hz. Recently, a direct relationship among STN oscillations at tremor frequency and tremor manifestation was discovered (Hirschmann et al. Brain 2013). This coherence at tremor frequency was also present between cortex and STN. However, it is not known whether DBS works most effective in patients with the highest LFP-EMG or EEG-EMG coherence profiles.
By studying coherence at 3 points of the motor pathway: cortex (EEG), basal ganglia nuclei (LFP) and muscle (EMG) before, during (LFP) and after DBS surgery in HMD we not only increase our understanding of the pathophysiology of HMD but also of the relation between neurophysiological and clinical changes in HMD.

Study objective

1. Investigate whether per-operative subcortico-muscular (LFP-EMG) coherence can be used as a predictor for favourable surgical outcome in DYS and PD tremor patients undergoing DBS surgery
2. Investigate whether pre-surgical EEG-EMG-coherence and cumulant density profiles alone predict the efficacy of DBS in DYS and PD tremor.
3. Investigate whether the change in pre- and post-surgical cortico-muscular (EEG-EMG) and intra-muscular (EMG-EMG) coherence can predict the efficacy of DBS in DYS and PD tremor.
4. Investigate whether intra-operative subcortico-muscular coherence assist in selecting stimulation contacts in DYS, ET and PD patients undergoing DBS.
5. Investigate whether there is a relation between cortico-muscular, subcortico-muscular and intra-muscular coherence and whether a combination of these three coherence methods can result in a strong predictor of DBS efficacy in DYS and PD.

Study design

A prospective cohort study with blinded endpoint evaluation will be conducted at the department of Neurology and Neurosurgery of the University Medical Center Groningen.

Study burden and risks

Besides the risks involved in DBS surgery for clinical care as usual, the risks involved for the participating patients are estimated to be negligible. During the recording interval that comprises circa 10 minutes and coincides with clinical testing, sterile recording electrodes are temporary connected to the implanted DBS leads. This procedure does not involve invasive techniques. For this reason there is no increased risk for intra-cerebral haemorrhage or other sequalae like seizures or brain shift. The theoretical risk of infection is assessed to be negligible since the electrodes which connect the implanted DBS leads to the EEG amplifier are sterile. Moreover, these electrodes are also used for teststimulation and the actual extra (temporary) connection made for measurements, will take place in the non-sterile environment. Additionally, the EMG electrodes are not located in the sterile operation area and therefore do not contribute to an infection risk. For above mentioned reasons, the DBS working-group concluded the patient*s risk for these intra-operative measurements to be marginal. The extra pre- and post-surgery investigations in PD and DYS will require approximately 2 hours of the patient*s time in which the subjects will undergo a brief neurological examination and EEG-EMG. In ET DBS battery replacement patients the added risk of measurements is expected to be marginal, since the same reasons mentioned above are applicable here. There are no potential benefits for the participating patients.

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 with Dystonia (DYS) or Parkinson's Disease (PD) who will be treated with DBS, and Essential Tremor (ET) patients with DBS in which the stimulator will be replaced operatively.
2. 18 years and older.
3. life expectancy longer than one year

Exclusion criteria

Any condition with a life expectancy less then 1 year, which would result in incomplete follow-up.

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	09-01-2015
Enrollment:	30
Type:	Actual

Ethics review

Approved WMO Date:	18-12-2014
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	03-03-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	24-09-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NL50575.042.14