Parkinson's disease and deep brain stimulation

Clinical effect and changes in the brain evaluated with SPECT

Annemette Løkkegaard, MD

This PhD dissertation was accepted by the Faculty of Health Sciences of the University of Copenhagen, and defended on May 11, 2007.

Official opponents: Liselotte Højgaard, Erik H. Danielsen, and Lars Forsgren, Sweden.

Tutors: Lene M. Werdelin and Lars Friberg.

Correspondence: Annemette Løkkegaard, Horserødvej 11, 1., 2100 Copenhagen, Denmark.

E-mail: alokkegaard@dadlnet.dk

Dan Med Bull 2007;54:232

ABSTRACT

This PhD dissertation is based on work I performed as a PhD student at Bispebjerg University Hospital in collaboration between the Department of Neurology, the Department of Clinical Physiology and Nuclear Medicine, Bispebjerg Hospital, and the Department of Neurosurgery, Rigshospitalet.

Parkinson's disease (PD) is a neuro-degenerative progressive disease characterised by the cardinal symptoms: bradykinesia and rigidity and tremor. Patients usually experience a good response to medication. However, after some years of treatment motor complications with fluctuations, hyperkinetic involuntary movements and off-periods may occur. In these patients Deep Brain Stimulation (DBS) in the subthalamic nucleus (STN) is reported to be an efficient treatment with effect on levodopa-responsive parkinsonian features as well as motor complications. Fifty-nine patients with late stage levodopa responsive PD underwent neurosurgical bilateral implantation of subthalamic stimulators. After the first 18 patients a new surgical procedure was introduced implying that targets were confirmed with intra-operative electrophysiologic recordings (MER). Evaluation included clinical assessment of motor symptoms with UPDRS, neuropsychiatric evaluation and imaging with SPECT rCBF and dopamine transporter SPECT before and after surgery.

The aim of this study was to investigate the clinical effect of DBS in PD and to reveal possible functional changes in the brain with SPECT imaging related to DBS in STN.

We found a good and sustained effect of STN-stimulation on the cardinal symptoms of PD: tremor, bradykinesia and rigidity as well as a clear reduction in OFF time and hyperkinetic movements. Notably the best ON phase was improved post-operatively, reflecting that stimulation and medication together was more effective than medication alone before surgery. It is suggested that the use of MER may have significantly improved the clinical results of surgery. However, also the pre-operative response to levodopa was predictive of the effect of stimulation. No serious adverse effects were encountered.

The specific binding of ^{123}I-FP-CIT was reduced equally in the STN-stimulated patients and a group of non-operated PD patients with advanced disease; our study does not support the notion that DBS STN should exert a neuro-protective effect by itself. Both surgery alone and DBS caused changes in relative rCBF. Normalisation of flow in the pre-motor cortex and the supplementary motor area was correlated to improvement in motor function as a result of stimulation. A relative reduction of flow in the pre-frontal cortex after surgery may be caused by the reduction in dopaminergic stimulation since medication was reduced considerably. A direct effect of STN-stimulation on prefrontal areas is also possible.