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**Parkinson's disease can be treated with deep brain stimulation (DBS) in the very advanced stage when patients develop medically refractory fluctuations and dyskinesia. A new publication suggests that the treatment is better than medical treatment already at an earlier stage.**

Parkinson's disease is a slowly progressive neurodegenerative disease which affects mobility until a state when the patients are unable to move without help. This comes with a dramatic loss of quality of life. So far DBS was only used for patients who have severe fluctuations and oscillate between severe akinetic and dyskinetic phases during the day. These patients had disease duration beyond 11 years. Previous controlled studies have shown that quality of life can be significantly improved for this patient group.

In a new German-French study published February 14<sup>th</sup>, 2013 in the New England Journal of Medicine (Schuepbach *et al.*, 2013) 251 patients were randomized to DBS or best medical treatment. The patients had a much shorter disease duration of 7.5 years. The main outcome was quality of life measured with a special Parkinson QoL-questionnaire (PDQ-39). DBS-patients had an improvement of 26% of their life quality versus no improvement in the medically treated group. Mobility under worst conditions (UPDRS II, without medication) was improved by 53%, activities of daily living (UPDRS II) were improved by 30% and Levodopa-induced complications were improved by 61% (UPDRS IV)(all significantly better than in the control group).

Safety parameters like the brief psychiatric rating scale and depression ratings were also significantly better in the neurostimulation than in the medication group. Memory and apathy were not different in the two treatment arms. Patients with neurostimulation had more side effects due to a higher number of mild side effects in this treatment arm. Suicides were found in 2 of the operated and 1 of the medically treated patients. Serious adverse events were common in both groups with 54,8% in the neurostimulation group and 44,1% in the medical treatment group. Among the 27 serious adverse events all completely resolved except for one which left a cutaneous scar.

Prof. Dr. Günther Deuschl, Head of the Department of Neurology, Kiel, Germany and German principal investigator of the study: 'The study showed surprisingly homogeneous results in favor of DBS compared with medical treatment. Almost all mobility parameters improved. The most important result is that quality of life of these patients and their social functioning was significantly improved. It is also meaningful that the operation has fewer side effects in this younger population than in advanced disease.' The outstanding effect of DBS on life quality is presumably due to the fact that patients can return after the operation to their normal planning of day which was no longer possible due to the disease.

Prof. Yves Agid, Paris, French principal investigator of the study emphasizes the excellent collaboration between the teams in the two countries and is also highlighting the generous support of the German and French sponsors (BMBF, PHRCN) as well as Medtronic as an industry partner. Agid says 'that the proof of concept of an early operation in patients with Parkinson disease is being definitively accepted, but it is important to keep in mind that the success of neurosurgery depends on both the strict inclusion of criteria of patients and the quality of an experienced multidisciplinary clinical team'. Both investigators hold the opinion that this study has the potential to change the international guidelines for the treatment of Parkinson's disease and will put DBS as a treatment option at a much earlier stage during the disease.

Background:

Deep brain stimulation is a treatment which needs a neurosurgical intervention to precisely position two electrodes in two very small regions deep in the brain called subthalamic nucleus. They are connected through cables to a subcutaneously positioned generator producing electrical pulses. The generator can be programmed through the skin with a special programmer.

The German and French teams of neurologists and neurosurgeons conducting this study have already a long track record of contributions to the field of DBS. Influencing studies were conducted by the German team on Parkinson's disease (Deuschl *et al.*, 2006, Witt *et al.*, 2008) and dystonia (Kupsch *et al.*, 2006, Volkmann *et al.*, 2012) and the French team on Parkinson's disease (Schupbach *et al.*, 2007) and dystonia (Vidailhet *et al.*, 2005, Vidailhet *et al.*, 2009). These country-specific networks of research centers have concentrated their efforts to complete this new study during the past 7 years. The academic Coordinating Center for Clinical Studies, Marburg, Germany was responsible for the biometry and data management and analysis.

Günther Deuschl and Yves Agid for the EARLYSTIM-study group

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