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POSTER SESSION 3

Surgical Therapy
Wednesday, June 16, 2004
8:30 AM–5:00 PM
Poster numbers 816–949

Authors present odd numbers: 11:30 AM–12:30 PM

Authors present even numbers: 4:00 PM–5:00 PM

P816

The impact of STN stimulation on brainstem excitability in parkinsonian patients

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Objective: To evaluate the effect of high-frequency stimulation of the subthalamic nucleus (STN HFS) on brainstem excitability in Parkinson's disease (PD).

Background: Current concepts of STN HFS emphasize the modulation of the thalamocortical output of the basal ganglia in PD. In contrast, descending basal ganglia projections to brainstem nuclei, such as the nucleus reticularis gigantocellularis (NRGC) and the nucleus reticularis pontis caudalis (NRPC) are often neglected.

Methods: We investigated STN HFS induced excitability changes of brainstem pathways by measuring spinal autogenic inhibition and auditory startle responses. For each experimental set up 10 PD patients with chronically implanted STN electrodes and ten age matched controls were studied. Patients were investigated after 12 hr withdrawal of antiparkinsonian medication with and without STN HFS (STIM ON/OFF). 1. Autogenic inhibition was studied by conditioning of the soleus H reflex by preceding gastrocnemius medialis nerve stimulation (2–10 msec ISI). This paradigm is assumed to reflect the activity of the NRGC [Delwaide et al., 1991]. 2. Ten startle responses evoked by an unexpected binaural sound (60 msec, 120 dB, 250–1,000 Hz) in ISI 2–3 min were measured in M. Orbicularis Oculi, M. Masseter, M. Sternocleidomastoideus, M. Biceps, M. Soleus respectively. 3. Soleus H reflexes conditioned by preceding auditory stimuli (30 msec, 100 dB, 500 Hz) in ISI 0–250 msec were investigated. The Startle reflex is suggested to indicate the excitability changes of the NRPC [Delwaide et al., 1993].

Results: In PD patients the abnormally reduced autogenic inhibition was significantly restored by STN HFS (ISI 6 msec: STIM OFF Mean/SE 95.4 ± 8.2%; STIM ON Mean/SE 76.1 ± 6.9%). The pathologically prolonged latency of the startle response onset was significantly shortened in the orbicularis oculi muscle after stimulation (STIM OFF Mean/SE 56.7 ± 1.9 msec, STIM ON Mean 52.7 ± 1.9 msec). The abnormally decreased fascilitation of the Soleus H reflex by auditory stimuli in PD was restored by HFS (ISI 125 msec: STIM OFF Mean/SE 127.7 ± 18.8%; STIM ON Mean/SE 237.8 ± 53.5%).

Conclusion: STN HFS restores the activity of brainstem nuclei such as the NRGC and NRPC. Here we present for the first time physiological evidence for a direct effect of subthalamic nucleus stimulation on subcortically driven brainstem circuits.

References

Delwaide PJ, Pepin JL, Maertens de Noordhout A. Short-latency autogenic inhibition in patients with Parkinsonian rigidity. Ann Neurol 1991;30:83–89.

Delwaide PJ, Pepin JL, Maertens de Noordhout A. The audiospinal reaction in parkinsonian patients reflects functional changes in reticular nuclei. Ann Neurol 1993;7:33:63–69.

P817

PC-based deep brain recording system for stereotactic and functional neurosurgery

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Objective: To develop a software for physiological targeting during stereotactic and functional neurosurgery using deep brain recording, to substitute with a personal computer (PC) the equipment for signal recording, display and processing, allowing automatic and graphic analysis of the recorded information even during the surgical procedure.

Background: Complex electronic equipment for electrical signal analog recording, display and processing is still used for deep brain recording during functional neurosurgery for movement disorders. However, the digital technology for signal recording and processing has already demonstrated its great advantages. Beside, the automatic and graphic possibilities offered by today's microcomputers can make the surgeons analysis easier, faster, more accurate and safer.

Methods: A PC-based software has been made to record up to 2 simultaneous signals with 12 bits accuracy by using an analog-digital converter card. The signal display is carry out on-line with its acquisition, emulating an oscilloscope up to 10 kHz of sampling rate. Signal-samples can also be analyzed off-line, processed and saved in the computer hard disk. The system allows some signal processing such as spike discrimination, window-amplitude discrimination, amplitude-histogram calculation, Fourier analysis, as well as an automatic integration of each recorded signal to quantify its general amplitude. The behavior of this integrated activity can be shown on a 2D- and 3D-representation of the electrode track into the brain, superimposed on the corresponding sagital, coronal and axial planes of a brain atlas, after their automatic scaling for each patient. It also allows the graphic representation of different lesions for ablative surgery.

Results: Several versions of this software have been developed since 1993. Each one of them has been validated and certified by the Cuban Medical Equipment Regulatory Agency. This system has already been used successfully in more than 600 stereotactic and functional neurosurgeries in Cuba, Chile and Spain. The clinical results of these surgical procedures have been published [1], showing the effectiveness of this computerized system too.

Conclusion: This software has already been used successfully for deep brain recording as an effective guide for the stereotactic and functional neurosurgery to control different symptoms of Parkinson's disease and other involuntary movement disorders. It substitutes with a PC complex electronic equipment, including automatic and graphic facilities that increase the accuracy and safety of the surgical targeting.

1. Alvarez LM, Macías R, Guridi J, et al. Dorsal subthalamotomy for Parkinson's disease. Mov Disord 2001;16:72–78.

P818

Deep brain stimulation in a patient on immunosuppressive therapy after renal transplant

A. Samii, J.C. Slimp, R. Goodkin (Seattle, Washington, USA)

Objective: To report a patient on systemic immunosuppressive therapy who successfully underwent thalamic deep brain stimulation (DBS) surgery for severe tremor 4 years after cadaveric renal transplant.

Background: There are no prior reports of DBS surgery to treat movement disorders in patients on systemic immunosupressive therapy after organ transplant.

Methods: All three authors provided extensive clinical care to the patient. We performed a detailed review of her medical records, laboratory and imaging data, detailed repeated neurological examinations, and videotaping of her movement disorder with written informed consent from the patient.

Results: (case report): A 36-year-old right handed woman with a 15-year history of progressive essential tremor presented to our movement disorders clinic for consideration of DBS. She had developed end stage renal disease (ESRD) in 1987 at age 20. Her ESRD was presumed to be due to a combination of hypoplastic kidneys, an electrocution accident at age 7,

and using high doses of daily aspirin for several years to treat migraine headaches. She underwent hemodialysis from 1987 to 1999. In 1999, she successfully underwent cadaveric renal transplant. Since transplant, she has received chronic immunosuppressive therapy with prednisone, cyclosporine, and mycophenolate mofetil (CellCept) with no bouts of rejection of the transplanted kidney. Her essential tremor was quite disabling, severely affecting her activities of daily living. After extensive discussions with the patient and her family, explaining the peri-operative risks of DBS surgery, she successfully underwent the implantation of a left thalamic DBS electrode and pulse generator in July 2003. There were no peri-operative complications. Post-operative healing was normal and no infections of the DBS hardware have occurred. She remains on the same systemic immunosppressive therapy regimen as pre-operatively. Left thalamic stimulation (intensity: 3.3 V, duration: 90 msec, rate: 130 Hz, cathode: #0 electrode, anode #3 electrode) has dramatically reduced her right upper limb tremor to almost complete resolution with a marked improvement in her activities of daily living.

Conclusion: Deep brain stimulation surgery for movements disorders may be safely performed in carefully selected patients on systemic immunosuppressive therapy after renal transplant.

P819

Unilateral subthalamic nucleus deep brain stimulation contralateral to thalamic stimulation in Parkinson's disease

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Objective: To report a patient with Parkinson's disease (PD) who underwent unilateral subthalamic nucleus (STN) deep brain stimulation (DBS) surgery contralateral to a previous thalamic DBS.

Background: Bilateral STN stimulation in carefully selected PD patients can improve motor function, reduce medication doses, and relieve motor fluctuations and dyskinesias. The effects of unilateral STN stimulation contralateral to thalamic stimulation have not been previously reported.

Methods: We performed detailed review of the patient's medical records, laboratory and imaging data, repeated neurological and Unified Parkinson Disease Rating Scale (UPDRS) motor examinations under various medication and stimulation conditions, and videotaping of motor exams with written informed consent from the patient.

Results: (case report): The patient developed left arm tremor in 1994 at age 62 as her first PD symptom. She underwent right thalamic DBS surgery in 1999 that resulted in complete resolution of left arm tremor. In 2001 she developed sudden electric shocks on the left side of her body and poor control of her left arm tremor. A break in the DBS electrode was detected and she underwent replacement of the right thalamic electrode in 2001 with resolution of left arm tremor. Her PD symptoms progressed and she developed severe motor fluctuations and disabling dyskinesias. With a daily intake of 1,400 mg of levodopa, 1,200 mg of entacapone and 24 mg of ropinirole in six divided doses, she had end of dose wearing off and severe dyskinesias. In July 2003, she underwent left subthalamic DBS surgery. Pre-operatively, with continuous right thalamic stimulation, her UPDRS activities of daily living (ADL) scores were 33 and 17 in the medication OFF and ON states, respectively. These ADL scores did not change significantly after left STN stimulation. In the medication OFF/stimulation OFF state, motor UPDRS scores pre- and post-operatively were 63 and 67, respectively. In the medication OFF state, right thalamic and left STN stimulation each markedly improved contralateral tremor and slightly improved contralateral limb motor performance. Left STN DBS allowed for mild reduction of medication doses, marked reduction of dyskinesia, and further improvement in motor UPDRS scores in the medication OFF state. However, there was no overall improvement of motor UPDRS scores in the medication ON state, ADL scores, gait, and postural stability.

Conclusion: STN stimulation contralateral to a previous thalamic stimulation in a PD patient reduced tremor and dyskinesia. It also improved motor UPDRS scores in the medication OFF state and allowed mild reduction in medication doses. However, it did not improve gait, ADL scores, or motor UPDRS scores in the medication ON state.

P820

Methodological concepts in subthalamic nucleus targeting: Controversies referring to deep brain stimulation (DBS) / neural transplantation

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Introduction: Subthalamic nucleus (STN) is a key structure in BG organization and is formed with about 300,000 excitatory neurons using glutamate as neurotransmitter. In PD this nucleus is disinhibited, leading to pathological excitation of its targets, GPi and SNpr. The contribution to this hiperexcitatory condition is influenced by thalamic parafascicular nucleus and pedunculopontine nucleus.

In normal conditions, there is a dopaminergic projection between STN and SNpc, added to a glutamatergic reciprocal projection. Increased GPi/SNpr outflow is believed responsible for many of the cardinal symptoms of PD.

Striatal transplantation of dopaminergic cells is capable of reverting the activity increase of cytochromeoxidase in entopeduncular nucleus and SNpr, but not in STN.

These premises offer an intuitive landscape about methodological contradictions that STN develops in therapeutic strategies based on lesioning, electrical stimulation and local drug infusion studies with GABA-agonists. Early failures with GDNF and cell therapy approaches contrast with DBS, which has shown remarkable in even late stages

Methods: To ensure backwards comparability and to facilitate interpretations of results, it is feasible to develop procedures to calibrate and perform a citation tracking concerning methodological and technical territorial scores in targeting STN referred to different therapeutic approaches: DBS and cell transplantation. A global statistical score discriminating among group differing in subzones areas is used, developing an algorithm of neuroanatomic premises.

Results/Conclusion: Evaluating the effect of transplanting foetal mesencephalic cells on animal models when introduced into polytopic targets (striatum and STN) and measuring the rotating activity induced by several drugs, no significant improvement was to be found when transplant were limited to just the subthalamus. On the other hand, correlation of therapeutic effect of DBS with anatomical electrode position, implies that DBS paliate symptoms by inhibiting STN activity directly, or by exciting afferent axons to the STN (f.i., from the globus pallidus) leading to indirect inhibition of subthalamic nuclear neuronal activity by release of GABA. Similarly, the axons of subthalamic nuclear efferents may be excited by DBS despite inhibition of proper neuronal activity within the nucleus. Other structures located in the subthalamus area have to be considered in this approach: fields of Forel or pallidothalamic fiber tracks and zona incerta.

Comparative premises: (1) In cell therapy or neural transplantation, dopaminergic cells implanted in STN, do not acquire a correct host-implantation relationship and migrate to zona incerta, entopeduncular nucleus and lateral nucleus of hypothalamus.(2) Distribution of TH+ cells was uniform, however, anti-TH antibodies staining was less intense in experimental models of STN transplantation.

From this it may be hypothesised that functional activity of DBS and topographic findings observed in neural transplantation confirm that beneficial effects of subthalamic nuclear stimulation, lesion or implantation depend on simultaneous modulation of several structures at once.

P821

Effect of high frequency stimulation of the subthalamic nucleus on extracellular glutamate and GABA in substantia nigra pars reticulata of freely moving hemiparkinsonian rats

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The subthalamo-nigral pathway strongly controls the output of the basal ganglia circuitry and has been implicated in movement disorders observed in Parkinson's disease (PD). High frequency stimulation (HFS, 130 Hz) of the subthalamic nucleus (STN) proves to be efficient for alleviating motor

symptoms in PD patients. However, the mechanisms underlying these clinical effects remain unknown.

Using intracerebral microdialysis in anaesthetized hemiparkinsonian rats we previously reported that STN-HFS induces an increase of nigral (SNr) GABA while glutamate remains stable [Savasta et al. The basal ganglia VII, 2002;581–590]. Using a similar approach, the objective of this study was to investigate whether such changes could also be detected in awake animals since general anaesthesia may interfere with a number of neurophysiological variables. A microdialysis probe and an electrophysiological stimulation probe were unilaterally implanted in SNr and STN respectively. Nigral extracellular concentrations of Glu and GABA were assayed by HPLC. Samples were collected every 8 min before (2 hr baseline), during (1 hr) and after (2 hr recovery) STN-HFS (130 Hz, 60 msec, 80 $<$ I $<$ 250 mA).

The preliminary results show that HFS-STN induces an increase of extracellular Glu while GABA remains stable. These neurochemical effects in SNr are currently being completed and should be confirmed. However, these data provide new arguments to identify STN-HFS mechanisms in PD.

P822

Predictive value of the Florida Surgical Questionnaire for Parkinson's disease (FLASQ-PD)

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Objective: To evaluate the effectiveness of the Florida Surgical Questionnaire for Parkinson's Disease (FLASQ-PD) and its constituent subscales at identifying appropriate candidates and potential future candidates for DBS surgery.

Background: Although many groups have speculated as to who will make the best candidates for DBS, there remains no standardized assessment tool. There is growing concern that as surgery for Parkinson's disease (PD) becomes more widely available, inappropriate patient selection could lead to an increased incidence of poor surgical outcomes. Health care professionals charged with the task of evaluating patients for potential DBS surgery will benefit from a quick and efficient screening tool such as the FLASQ-PD.

Methods: The FLASQ-PD is a 5-section protocol that includes: (A) probable diagnosis of idiopathic PD, (B) potential contraindications, (C) general patient characteristics, (D) favorable/unfavorable characteristics, and (E) medication trial subscores. The questionnaire which was previously utilized in a multi-center trial was designed to screen for the best surgical candidates. The current study utilized a retrospective analysis of 174 consecutive patients presenting for a surgical screening at a single center (University of Florida). All patients were examined by a movement disorders expert, and assigned to one of four clinical categories (1- Idiopathic PD ready for surgery, 2- Idiopathic PD- not ready for surgery, but potentially a future candidate, 3- Idiopathic PD- not a surgical candidate, 4- not idiopathic PD, and, therefore, not a surgical candidate). The charts of the patients were then reviewed by a blinded investigator who completed the FLASQ-PD for each patient. Discriminant function analysis was used to assess whether the questionnaire could discriminate between surgical and non-surgical candidates.

Results: Of the 26 questions on the FLASQ-PD no single question correctly classified candidates more than 72.9% (mean 64%) of the time. When performing discriminant function analysis using two groups (ready for surgery +potential candidates vs. no surgery + not PD), 83.3% of patients were correctly identified using the five combined subscales, Wilks' _ = 0.56, _2(5, 173) = 97.5, $P < 0.001$. The discriminant function was characterized by high loading of the "met PD criteria" and "contraindications" subscales. The individual subscales were not as effective as the combined five subscales at identifying candidates (met PD criteria 73.6%, contraindications 74.7%, patient characteristics 70.1%, potential contraindications 65.5% and medication trial 64.4% ($P = 0.013$)).

Conclusion: Discriminant function analysis suggests that the FLASQ-PD may be useful for discriminating good DBS surgical candidates for Parkinson's disease, with a high proportion of candidates (83%) being correctly classified. The results of this retrospective pilot study will need to be substantiated by prospective trials.

P823

New treatment paradigm in dystonic movement disorders: Multifocal deep brain stimulation

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Objective: To evaluate the usefulness of deep brain stimulation of different targets and their comparative efficacy in patients with dystonic tremor and secondary dystonia.

Background: There has been a renaissance of functional stereotactic surgery for treatment of dystonia. Chronic deep brain stimulation (DBS) of the posteroventral lateral globus pallidus internus (GPi) has been shown to provide substantial benefit in patients with idiopathic generalized dystonia. In the rare case, patients with unusual manifestations of dystonia have also been reported to benefit from thalamic ventrolateralis posterior (VLp) DBS.

Methods: Six patients with medically refractory dystonia were selected for this prospective study. There were four women and two men. Three patients had secondary dystonia including peripherally-induced posttraumatic hemidystonia, head tremor secondary to head injury, and upper limb tremor associated with choreoathetosis due to cerebral palsy. The other patients had primary dystonia with prominent tremor involving the head (1), the neck and upper extremities (1), and the trunk when standing (1). All patients underwent bifocal implantation of quadripolar DBS electrodes in the GPi and the VLp, either bilaterally (5 patients) or unilaterally (1 patient) in the same operative session. Electrodes were externalized for test stimulation for several days.

Results: There were no adverse events. In four patients, it was possible to determine the more effective stimulation site during test stimulation. Rating scores showed that better improvement was achieved with pallidal stimulation in the three patients with primary dystonia, and that the posttraumatic dystonic head tremor was improved more markedly with VLp stimulation. No improvement of dystonia was observed in the two other patients with secondary dystonia during test stimulation, and these two patients underwent chronic alternating stimulation of the GPi and the VLp after implantation of pacemakers.

Conclusion: Multifocal DBS is a useful tool in patients with unusual manifestations of dystonia and those with secondary dystonia. It has been proven to be safe and effective in this series of patients.

P824

Deep brain stimulation for distressful belching

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Objective: In the present study we tested the hypothesis that DBS of the internal pallidum might be effective in a patient with neuroacanthocytosis suffering from an intractable and severe belching.

Background: A 32-year-old Algerian with an 8-year history of choreoacanthocytosis presented with recurrent distressing tasteless belching, socially extremely invalidating and resistant to medical treatment. It was preceded by episodes of short repetitive dyspnea evoking breathing dystonia. The patient also exhibited severe and recurrent tongue biting as well as dystonic and choreic movements of the lower limbs. Videofluoroscopy showed normal deglutition and slight hypotonia of the inferior esophageal sphincter (IOS) that was confirmed by esophageal manometry. Electromyography of the diaphragm did not disclose any diaphragmatic flutter but did show repetitive recurrent arrhythmic prolonged contractions of both diaphragmatic domes concomitant with breathing irregularities.

Methods: After receiving the patient informed consent, deep brain stimulation (DBS) of the internal pallidum was administered. Under general anesthesia and ventriculographic control, one electrode for chronic stimulation was implanted into the ventro-latero-basal part of each GPi. The following bilateral monopolar stimulation settings were used: 2 negative (lower) contacts, 3.0 V at both sites, 130 Hz frequency, pulse width 90 msec.

Results: Two days after the onset of stimulation, a dramatic decrease was observed not only in belching and dystonic breathing but also in the choreic

and dystonic movements involving the lower limb and axis, as well as the tongue. Polygraphic recordings under video control performed 3 weeks after surgery revealed that both the mean number of episodes of belching and dystonic breathing were statistically decreased ($P < 0.0001$). DBS was also effective on the facial dyskinesia responsible for tongue biting and on other distal choreic and dystonic movements occurring in the lower limb and the back.

Conclusion: Our data suggest that DBS of the GPi could be proposed for both axial and distal choreic syndromes threatening the vital prognosis.

P825

Subthalamic nucleus deep brain stimulation for Parkinson's disease using magnetic resonance images for localization with and without microelectrode recording: A comparative study of outcome

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Objective: Various targeting methods are described in the literature for subthalamic nucleus deep brain stimulation (STN-DBS) according to the facility of the hospital and the familiarity of the physician. We compared the outcome of the patients in our institute who underwent STN-DBS with or without intra-operative microelectrode recording (MER).

Methods: From Feb. 2002 to Nov. 2003, 24 Parkinsonian patients were underwent STN-DBS in our institute. Thirteen patients who followed for at least 3 months post-operatively were divided into two groups for outcome comparison. Group A (STN-DBS without MER) included 7 patients (3 male and 4 female), with a mean age of 60.7 year-old (SD 10.1). Group B (STN-DBS with MER) included 6 patients (2 male and 4 female), with a mean age of 56.8 year-old (SD 11.5). A core assessment program included: acute levodopa test for Unified Parkinson's Disease Rating Scale (UPDRS) with video tapping, timed-test, autonomic nervous system evaluation, mini-mental status examination (MMSE), and magnetic resonance images (MRI), was conducted pre- and post-operatively in all patients.

Results: The average Hoehn and Yahr stage in groups A/B were 3.8/4.0 respectively. The mean followed duration in groups A/B were 7.3/5.2 months respectively. Permanent electrodes for STN-DBS were properly placed in both groups. The average coordinates of the tip of the permanent electrode detected by post-operative MRI in according to the mid-anterior and posterior commisure in both groups A/B were X = 8.1/10.6 mm (lateral), Y = 4.3/4.1 mm (posterior), Z = 5.9/6.9 mm (inferior), respectively. Under the state of medication "Off" in post-operative follow up, the percent changed when DBS "On" versus "Off" was calculated and was compared to pre-operative medication "On" versus "Off" state. In group A, the post-operative UPDRS total and motor scores were improved by 29.9% ($P = 0.01$) and 30.9% ($P = 0.02$) respectively. The levo-dopa equivalent daily dose (LEDD) was decreased by 15.5% ($P = 0.03$). In group B, the post-operative UPDRS total and motor scores were improved by 44.3% ($P = 0.00002$), and 40.7% ($P = 0.0004$) respectively. The LEDD was decreased by 51.9% ($P = 0.01$).

Conclusion: Subthalamic nucleus deep brain stimulation is a promising surgical modality for advanced PD. The use of MER is a helpful adjunct to refine the surgical target for permanent electrode implantation and to enhance the surgical outcome.

P826

Correlation between the patient's ability to perform motor tasks, their perception of this ability, their mood and affect, and the relationship of these with levodopa and deep brain stimulation in Parkinson's disease

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Objective: To determine: 1) whether there are some patients with PD whose ability to perform motor tasks does not correlate with their perception of how able they are, 2) the relationships between this perception, mood/affect and levodopa, and 3) whether these relationships change following DBS in individual patients.

Background: Patients with PD are assessed before and after functional neurosurgical procedures using the CAPSIT-PD. Over several years of carrying out these assessments, it had been observed that there were some patients who felt that they would be unable to perform the motor tasks involved and yet who could, when asked to do so, carry out these tasks quite well. It was also noted that some patients' perception of their ability improved significantly following levodopa intake even though their performance of motor tasks did not. Although this phenomenon has been investigated in the past, it has not been explored within the context of DBS surgery and may have an impact on the patients' perception of the outcome of such surgery, particularly if their PD medications are reduced substantially post-operatively.

Methods: Patients were assessed before, and 6 months after, DBS surgery on the subthalamic nucleus (STN), Globus Pallidus interna (GPi) or Thalamus using the CAPSIT-PD and a Visual Analogue Scale (VAS) to assess aspects of mood, perception of 'on/off' state, and perception of physical ability. The timed motor tasks and VAS were undertaken with the patient in the practically defined off state and then every 20 min until they had achieved a subjective and objective 'best on' state. The assessment then continued until they perceived themselves to be declining towards the off state and/or when the time of motor task completion began to increase.

Results: Twenty-six patients with PD were assessed as part of the functional surgery programme. Of these, approximately half went on to have DBS surgery, either at the GPi (n = 4), Thalamus (n = 1), or STN (n = 7). Preliminary analysis of the data confirms that there are differences in the correlation between some aspects of mood, perception of ability and levodopa from one patient to another. Further analysis is in progress to determine whether these relationships change following DBS surgery.

Conclusion: There are differences between patients with regard to the correlation of their perception of their physical ability and their actual ability to perform motor tasks and the relationship of this to levodopa intake. Further work is needed to determine whether this affects the patients' perception of the outcome of DBS surgery.

P827

Effect of propofol anesthesia on the firing pattern of GPi neurons in generalized dystonia

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Objective: To assess the effect of propofol anesthesia (PA) on the discharge behavior of neurons in the internal globus pallidus (GPi) of patients undergoing implantation of deep brain stimulation (DBS) electrodes into the GPi to treat idiopathic torsion dystonia (ITD).

Background: The current pathophysiological model of basal ganglia disorders relates akinesia to an increase and hyperkinesias to a reduction of GPi-firing frequency. In agreement with this concept, abnormally low discharge rates of GPi neurons were found in an animal model of dystonia and during intraoperative microelectrode recordings in patients with ITD. Pallidal surgery for ITD often requires general PA. A recent report ascribed the observed changes in spontaneous discharge behavior of GPi neurons to the effect of PA and challenged the concept of reduced GPi activity in dystonia. However, in this study neuronal recordings were compared across patients with different etiology and severity of dystonia being operated under PA or local anesthesia. Here we analyze the effect of altering the level of PA during ongoing neuronal recordings in GPi of patients with ITD.

Methods: We performed microelectrode recordings within GPi of 4 patients with ITD [age: 15–59 years, all DYT1 negative, BFMDRS: 42.5P (range 20–101.5)]. All patients were operated under general anesthesia with propofol and remifentanyl. In selected neurons with stable baseline recordings for several minutes PA was stopped for a period of 3–11 min until first clinical signs of arousal were observed. Off-line analysis using threshold spike detection and template matching, controlled by cluster analysis with principal component analysis, was performed to assure single unit discrimination. Neuronal discharge patterns with and without PA were compared by mean firing rates (1 sec intervals), interspike interval histograms (ISIH) and autocorrelation histograms (ACH). Changes in the discharge rates of individual cells were tested for significance using Wilcoxon-test for paired samples.

Results: Nine of 14 neurons, which could be followed for a sufficiently long period after stopping PA, were analyzed. Three neurons showed no

change in mean discharge rate, while 2 neurons presented a significant increase and 4 neurons a decrease. A subset of 4 neurons could be recorded after re-initiation of PA. Only 1 of these cells showed a reversible effect on discharge rate. The ISIH as well as the ACH of individual cells showed no relevant change of the discharge pattern related to level of PA.

Conclusion: PA has no consistent effect on firing frequency and discharge patterns of GPi neurons in patients with ITD. The observed small, but sometimes significant changes in discharge rate over time may rather reflect long-term fluctuations of spontaneous neural activity in ITD than a specific action of PA or the level of consciousness per se.

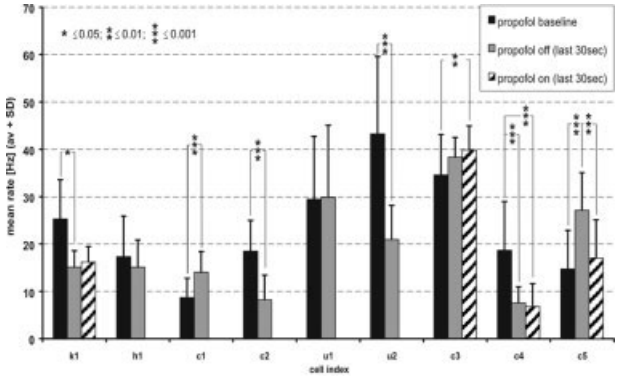

FIG. 1 (P827).

P828

Effects of stereotactic neurosurgery on postural instability and gait in Parkinson's disease: A systematic review

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Objective: To systematically review studies that examined the effects of globus pallidus (GPi) or subthalamic nucleus (STN) surgery on postural instability and gait disability (PIGD) in Parkinson's disease.

Background: Stereotactic surgery for Parkinson's disease has been aimed at different nuclei, including the thalamus, GPi and STN, and has been performed with different techniques and approaches including: unilateral lesioning, bilateral lesioning, unilateral stimulation and bilateral stimulation. There is overall agreement that thalamic stereotactic surgery is not effective in improving PIGD. Stereotactic surgery aimed at the GPi or STN might be more effective, but the precise effects remain unclear.

Methods: In this review we included studies that examined the effects of GPi or STN surgery on PIGD at 3, 6 or 12 months after surgery using either the UPDRS (items 13–15, 27–30), timed tests (stand-walk-sit-tests and timed walking tests), posturography or quantified gait analysis to assess PIGD. Most studies examined the effects of unilateral pallidotomy, bilateral GPi stimulation or bilateral STN stimulation using the UPDRS to assess PIGD. We therefore only performed a meta-analysis for these studies. We expressed the effects of surgery on PIGD as the difference score between pre-and post-operative UPDRS values. For each study included in the meta-analysis we recorded the following mean baseline clinical characteristics: (a) baseline off-state PIGD score; (b) baseline on-state PIGD score; (c) age at disease onset; (d) disease duration; (e) age at surgery; (f) magnitude of PIGD levodopa response preoperatively; and (g) postoperative % change in medication.

Results: There were no major differences in the baseline clinical characteristics of patients recruited for different types of surgery. However, medication was reduced only after bilateral STN stimulation, whereas it remained approximately unchanged after both unilateral pallidotomy and bilateral GPi stimulation. Unilateral pallidotomy, bilateral GPi stimulation and bilateral STN stimulation were all effective in improving PIGD in the 'off' state. Bilateral STN stimulation and bilateral GPi stimulation were significantly more effective than unilateral pallidotomy. For bilateral GPi stimulation and bilateral STN stimulation the effects approximately equalled the effects of medication pre-operatively, whereas for unilateral pallidotomy there was a trend for these effects to be smaller than the effects of medication pre-operatively. Unilateral pallidotomy, bilateral GPi stimulation and bilateral STN stimulation also improved PIGD in the 'on' state, but these improvements were smaller than those observed in the 'off' state.

Conclusion: Unilateral pallidotomy, bilateral GPi stimulation and bilateral STN stimulation were all effective in improving PIGD. The effects of the remaining types of surgery on PIGD remains unclear.

P829

Subthalamic nucleus deep brain stimulation effect in elderly patients with Parkinson's disease

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Objective: We compared clinical, cognitive and quality of life outcomes following sub thalamic nucleus deep brain stimulation (DBS) in 2 groups of patients with Parkinson's disease (PD) (patients older than 65 years at time of surgery and younger patients).

Background: Bilateral DBS provides major benefit to patients with advanced PD. Age is a key factor to consider when determining surgical candidacy. It has been suggested that elderly PD patients could be less improved after surgery and could have a higher risk of post operative complications.

Methods: We studied 16 older (69 $\pm$ 2 years, range: 66–73) and 31 younger (54 $\pm$ 7 years, range: 40–64) PD patients. Motor function (all parts of UPDRS), neuropsychological tests and quality of life (PDQ-39) were performed before surgery and after 3 and 6 months. After surgery, motor disability score (UPDRS part III) was evaluated after stimulation had been switched on during two different conditions: OFF medication (after at least 12 hr of dopaminergic treatment discontinuation) and ON medication (after suprathreshold levodopa dose). The mean variations (difference of parameters between 6 or 3 months and before surgery) were compared between the 2 groups of patients.

Results: Before surgery, UPDRS part III off medication was significantly greater in younger PD patients compared with aged one ($P = 0.04$). There was no significant difference in other parameter between the 2 groups. After surgery, mean variation of items 32 to 42 of UPDRS (complications of therapy) was significantly greater in older patients than in younger (-10 ± 3 vs. -6 ± 4 at 3 months, $P = 0.01$). Mean changes in part I, II and III of UPDRS were similar in the 2 groups. There were no significant mean variations in neuropsychological tests but older PD patients tended to have slower executive functioning performance. Despite the lack of significance, mean changes in PDQ-39 were greater in older PD patients. Only older patients experienced surgical complications (2 intracranial haemorrhages, and 1 death). Transient post operative confusion, apathy and depression were more frequent in elderly patients.

Conclusion: Elderly PD patients experienced more adverse events after DBS but exhibited more marked improvement in motor complications and a trend toward better quality of life outcome compared with younger patients.

P830

Improved motor responding, but central slowing, after bilateral subthalamic nucleus stimulation in patients with Parkinson's disease

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Objective: To assess the effect of bilateral subthalamic nucleus (STN) stimulation on simple reaction time (SRT) and complex reaction time-(CRT) performance.

Background: STN hyperactivity is a pathophysiological hallmark of Parkinson's disease (PD). Decreasing its activity by high frequency stimulation (HFS) alleviates Parkinsonian motor symptoms. However, the effect of STN HFS on cognitive performance has never been formally

studied. Reaction time (RT) performance is often used in PD to evaluate motor and cognitive functions.

Methods: We evaluated seventeen PD patients with STN stimulators. We conducted pre-operative and post-operative assessments of motor function, functional performance and neuropsychological parameters. We measured SRT and CRT (go/no go task) during four post-operative conditions with stimulation (stim) and medication (med) on and off: stim on-med on, stim on-med off, stim off-med off and stim off-med on.

Results: STN stimulation improved motor disability, functional performance and the depression score, but a significant slowing (50.6%) of mental speed occurred as reflected in the corrected CRT (CCRT) score. The latter was independent of dopaminergic medication.

Conclusion: These data suggest that treatment of STN hyperactivity by HFS improves motor function, confirming earlier reports, but negatively influences the speed of cognitive processing. This is most probably due to interference with the activity of the basal ganglia-thalamocortical pathway. This needs further clarification in future studies. Caregivers should be aware of this negative effect as STN HFS is widely applied nowadays.

P831

Spinal cord stimulation in patients with primary orthostatic tremor

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Objective: To study the effects of chronic spinal cord stimulation (SCS) on medically refractory primary orthostatic tremor (POT).

Background: POT is characterized by an intense sensation of unsteadiness and shaking of legs and trunk when standing quiet. The diagnosis is confirmed by a typical 14–16 Hz burst activation pattern in EMG recordings. If medical therapy fails, the patient's daily activities can become very limited.

Methods: Quadripolar plate electrodes (Symmix, Medtronic) were implanted via a limited laminotomy approach with the patients in prone position under intravenous analgesia. Electrodes were externalized for test stimulation for several days. Two patients with POT, a 58-year-old woman and a 72-year-old man were selected for this study. The duration of POT was 10 years in patient 1, and 8 years in patient 2. Patient 1 also suffered from diabetic neuropathic pain. Medical therapy was not effective in both instances. The prospective study protocol included timed measures of the ability to stand still combined with EMG tremor recordings.

Results: Intraoperative electrical stimulation produced paraesthesiae of both legs. There were no adverse events. Test stimulation showed that the abilty to stand still improved markedly in both patients. The electrodes then were internalized and connected to implantable programmable impulse generators (Itrel III, Medtronic). Stimulus parameters were gradually adjusted to maximum effect on unsteadiness. Patient 1, who was able to stand still for a maximum of 2 min preoperatively, became free of symptoms when standing (amplitude 1.0 V, frequency 100 Hz, duration 210 μsec). In patient 2, the ability to stand still was 10 sec preoperatively, and it increased to 150 sec (3.7 V, 220 Hz, 210 μsec). In both patients, clinical improvement was stable at 1-year follow-up.

Conclusion: Chronic SCS is useful in patients with medically intractable POT. Its effects may be mediated by the modulation of the oscillators responsible for POT via activation of the dorsal columns.

P832

Quality control procedure for stereotactic magnetic resonance imaging during neurosurgery of movement disorders

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Background: A critical step in all stereotactic procedures remains accurate target localization. The outcome of the surgery for deep brain stimulation is directly based on imaging accuracy.

Objective: To present the technical requirements for implementing a stereotactic methodology using 3D MR imaging alone for deep brain stimulation, of GPi and STN.

Methods: Deep brain stimulation systems were stereotactically implanted using Leksell G frame and MRI, under general anesthesia in the STN (1 patient) and in the GPi (80 patients) with clinical improvement. The accuracy of the entire procedure was validated by an immediate postoperative stereotactic MRI. Electrodes were checked to be on the selected target in all the patients.

Results: During a stereotactic operation for DBS the following steps must be constantly controlled: (1) the rigidity of the stereotactic frame and dedicated MRI location box; (2) fixation of the adapter and alignment of the frame in the MR unit; (3) absolute inhibition of movement during acquisition (general anesthesia if necessary), (4) control of distortion with a regular check of the gradient fields if necessary (rigorous maintenance protocol) and use of the frame box as a fantom to check the distortion rate (dimensions, forms), (5) a validation of merging methodology if used (pixel size, image orientation, brain movement). The reliability of the MRI-based targeting could be improved using an adapted slice thickness (no more than 2mm for small structures), an isometric pixel size in the plane of targeting (x,y) (square matrix, scan percentage of 100%), and preferably no gap between slices, and no overcontiguous slices.

Conclusion: We designed and validated the use of a stereotactic methodology using 3D MR imaging alone for deep brain stimulation procedure. The procedure is safe (very low morbidity), accurate (100% of electrodes are positioned on the chosen target) and short (30 min per electrode).

P833

Treatment of Parkinson's disease by deep brain stimulation: Evaluation of an MRI-based surgery under general anesthesia

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Background: Placement of deep brain stimulation (DBS) electrodes in brain structures is often a lengthy procedure. Most centers use physiologic monitoring, including microelectrode recording (MER) and macro-stimulation, for increasing the precision of electrode placement. The vast majority of literature regarding DBS, dictates the procedure to be performed in a patient in the *off* state with minimal or no sedation.

Objective: To describe a neurosurgical technique for implanting stimulation electrodes in Parkinson patients under general anesthesia, without the resort to MER and clinical testing, based only on stereotactical MRI and anatomical direct localization of the GPi.

Methods: Eight patients suffering from Parkinson's disease were treated by DBS of the GPi (1-year follow-up). Surgical procedure was performed under general anesthesia using the Leksell G frame. Target coordinates were calculated on a 1.5-T MRI system acquisition. The immediate post-operative stereotactical MRI under general anesthesia should be a crucial prerequisite to check the reliability of MR acquisition (magnet stability) and the exact localization of each electrode reflecting the precision of the entire procedure.

Results: This technique allowed us to reduce the duration of the operation: 4 hr including general anesthesia, frame fixation, MRI acquisition, implantation of 2 electrodes under radioscopic control, immediate post-operative stereotactic MRI and frame removal. Surgery-related morbidity was very low with a 0% hemorrhage rate. Electrodes were checked to be on the selected target for all the patients. Improvement of Unified-Parkinson's disease Rating scale motor score after 12 months of DBS off medication, was 28.48%, without any neuropsychological or psychiatric secondary effects. Speech, akinesia, rigidity, tremor, and postural stability improved.

Conclusion: The advances of 3D-MR imaging allow to propose the electrode implantation for DBS for Parkinson's disease under general anesthesia without the resort to any complementary intra-operative techniques. The post operative course confirmed the efficiency and the good tolerance of this treatment. It is comparable to published results with long lasting surgery (8–12 hr) using MER and macrostimulation.

P834

Apomorphine continuous subcutaneous infusion and bilateral subthalamic stimulation in the treatment of advanced Parkinson's disease: A pilot comparative study

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Objective: To compare the effectiveness of STN-DBS and APM-csi in the management of motor fluctuations and dyskinesias.

Background: Subthalamic Nucleus Deep Brain Stimulation (STN-DBS) and Apomorphine (APM) continuous subcutaneous infusion (csi) are effective approaches to relieve motor fluctuations and dyskinesias, but no comparative studies have been performed so far.

Methods: We studied 18 patients with advanced PD included in the STN-DBS waiting list: patients for which the date for surgery was programmed within one year from the start of the study were included in the surgical arm; patients with a longer waiting time were proposed for APM-csi. Nine patients were included in each group. Patients were assessed at baseline and at one year follow-up. Unified Parkinson Disease Rating Scale (UPDRS) and the Abnormal Involuntary Movements Scale (AIMS) were evaluated every one hour, during eight hours by the same physician. Patients filled home diaries of motor fluctuations and dyskinesias during three consecutive days preceding each admission.

Results: Demographic and clinical characteristics of the patients of each group were not significantly different. Seven patients of the APM-csi group and nine of the STN-DBS group completed the study. Two patients on APM-csi abandoned the treatment after 2 months (due to difficulty in pump management in one patient and to visual hallucinations and delusion in the other) and were not included in the statistical analysis. Mean stimulation parameters values were: amplitude 3.5 V (range 2.8–4.0), pulse width 70 msec (range 60–90)/frequency 160 Hz (range 130–185)). The mean APM dose was 92.3 (range 80–120) mg per day. The duration of the infusion was 16 hr the day. Oral antiparkinsonian medication was reduced by 43% in the STN-DBS group and by 70% in the APM-csi group. "On" time duration increased by 43% in the STN-DBS, and by 63% in the APM-csi group. STN-DBS reduced the "worst off" UPDRS III score by 58% and APM-csi by 53%. STN-DBS reduced dyskinesias severity by 59% and dyskinesias duration by 62%. In patients on APM-csi there were no significant changes in severity and duration of dyskinesias. The AIMS score improved in three patients, was unchanged in one, and worsened in three, whereas the duration of dyskinesias showed a global increase of 31%. In the APM-csi group two patients presented persistent and bothersome subcoutaneous nodules. Neuropsychiatric side effects appeared in two patients. In the STN-DBS group three patients presented speech impairment and two, dystonic postures of one leg.

Conclusion: Both STN-DBS and APM-csi are effective in the treatment of advanced PD. Both treatments markedly reduced motor fluctuations, reducing the duration and the severity of off time. STN-DBS improved dyskinesias in all patients, whereas the effect of APM-csi on dyskinesias was inconstant. Results suggest that in patients with disabling dyskinesias STN-DBS rather than APM-csi should be considered the preferential treatment.

P835

Lewy body dementia in a patient with Parkinson's disease developing cognitive changes while under subthalamic stimulation: A clinicopathologic study

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Objective: To show that cognitive deterioration in patients with Parkinson's disease (PD) in which bilateral subthalamic stimulation (STN-DBS) has been performed may be due to the progression of the neurodegenerative process rather than the stimulation by itself.

Background: STN-DBS improves cardinal symptoms of PD. This therapy rarely induces cognitive changes and worsens dementia in PD and consequently patients with dementia are excluded from such therapy.

Case Report: A patient with advanced PD presented medically untreatable motor complications after eleven years from the onset of symptoms. He was considered to be a good candidate for STN-DBS in spite of being 74 years-old. Pre-surgical neuropsychological performance, assessed by Rey's Auditory-Verbal Learning, Judgment of Line Orientation, Trail Making, Stroop, and phonetic and semantic verbal fluency, was normal. Three months after STN-DBS the patient showed disappearance of motor fluctuations and dyskinesias. An improvement in the activities of daily living score, and a 70% reduction in dopaminergic medication was observed. Neuropsychological assessment did not evidence any cognitive change. On the ensuing 2 years, motor performance and dopaminergic medication remained stable. Shortly later, the patient developed mild depressive symptoms and diurnal somnolence. At 3 years follow-up, the patient presented fluctuating spatial and temporal disorientation, impaired verbal learning, apraxia, aphasic deficits, and visual agnosia. These deficits progressed and in the following months hallucinations, paranoid ideations and aggressiveness appeared. Atypical neuroleptics were tried, but with little benefit. In order to rule out a relation between cognitive and behavioural changes and STN-DBS, stimulators were switched-off for one month. During this time, parkinsonism was aggravated but no change in mental status was detected. Later in the course, the patient received galantamine showing an important improvement of psychiatric symptoms and cognition. Four years after surgery the patient died from a bronchopneumonia.

The brain pathologic findings showed changes typical of PD. In addition abundant Lewy bodies were found in the amygdalar complex and were abundant in several cortical areas. No Alzheimer type pathology was detected. The pathological diagnosis was diffuse Lewy body disease. The electrode tips were placed within the limits of the STN in both sides.

Conclusion: We report a patient with advanced PD successfully treated with bilateral STN-DBS. Three years after surgery he became demented and at autopsy was found to have diffuse Lewy body disease. While demented, STN-DBS continued to improve the parkinsonism but did not seem to have any significant influence upon the existing cognitive changes and behavioural disturbances. Although the long-term effects of STN-DBS on cognition are not well established, this case report suggest that the development of dementia in this patients was due to progression of the neurodegenerative process rather than to an effect of subthalamic stimulation.

P836

Bilateral STN stimulation in Parkinson's disease leads to a decrease in mental speed

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Objective: To investigate the cognitive effects of bilateral subthalamic nucleus (STN) stimulation in Parkinson's disease.

Background: Bilateral subthalamic nucleus stimulation has proven an effective surgical therapy for PD patients. Until now only a few studies have reported the neuropsychological effects of the surgery.

Methods: Preoperatively and six months postoperatively we administered a comprehensive neuropsychological examination to 58 PD patients who received bilateral STN stimulation.

Results: Six months after surgery, patients scored significantly lower on three measures of word fluency. Moreover, the score on the Mattis Dementia Rating scale (DRS), a cognitive screening task was significantly lower. This was not only due to the subscale initiation and perseveration, which is highly determined by a category fluency measure but also to the subscale attention. Furthermore, patients scored significantly lower on the Stroop Color Word test, which measures mental speed and selective attention. Finally, patients reported significantly less symptoms of depression after surgery. The decrease in word fluency and on the DRS is significantly correlated with a decrease in basic mental speed, but not with age, disease duration nor with mental status at baseline. Correlation with motor scores are not yet available, but will be presented at the poster.

Conclusion: Bilateral STN stimulation in PD leads not only to a slight decrease in word fluency, but also to a slight deterioration on a cognitive screening test. This seems to be related to a decrease in basic mental speed.

P837

Comparative effects of unilateral STN vs. GPi DBS on movement time, dexterity, and reaction time

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Objective: We sought to assess and compare the effects of unilateral DBS of the STN and GPi on upper extremity motor function. An automated device was used to measure movement time, dexterity, and reaction time in an objective, quantitative manner.

Background: Deep brain stimulation (DBS) is an effective treatment for selected patients with disabling Parkinson's disease (PD). The two main targets for DBS are the subthalamic nucleus (STN) and the globus pallidus internus (GPi), although it has not been established whether stimulation at one target is superior to the other. In addition, the extent to which preoperative variables such as age and medication responsiveness predict postoperative stimulator efficacy remains unclear.

Methods: Thirty five patients with advanced levodopa-responsive PD enrolled in a prospective, randomized study of staged DBS of the STN versus GPi were studied using an Axon instruments movement monitor (model MM-1; Foster City, CA). This is an automated device that assesses upper extremity movement and reaction times by measuring hand movements in response to audible and visual queues. The device also measures dexterity in a knob-turning task and has been used previously in similar paradigms. Three to six months following unilateral STN or GPi stimulator implantation, we assessed contralateral and ipsilateral movement with the stimulator on or off, in both the off-medication and on-medication states. In addition, we examined the extent of post-operative improvement as a function of pre-operative patient age and medication responsiveness.

Results: Stimulation of the STN (18 subjects) in the off-medication state significantly decreased contralateral movement time ($-28\% \pm 7.4\%$ [mean $\pm$ SE], $P < 0.01$ by Newman-Keuls *post-hoc* test) and improved dexterity ($43\% \pm 26\%$, $P < 0.05$), but did not significantly affect reaction time, when compared with the off-medication, off-stimulation state. Similarly, stimulation of the GPi (17 subjects) significantly decreased contralateral movement time ($-17\% \pm 13\%$, $P < 0.05$) and improved dexterity ($42\% \pm 25\%$, $P < 0.05$), but it had no effect on reaction time. The extent of improvement did not differ between the two targets ($P = 0.75$ and 0.38 by three-way ANOVA for movement and dexterity, respectively). In one instance, movement time for patients treated with GPi DBS, there was also a significant ipsilateral benefit of stimulation ($-15\% \pm 8.6\%$, $P < 0.05$). For contralateral dexterity (but not movement), an additive improvement was noted when patients received both medication and stimulation compared to stimulation alone. The degree of benefit from stimulation of either the STN or GPi was independent of age and the extent of preoperative medication responsiveness.

Conclusion: Our findings suggest that DBS of the STN or GPi results in a similar degree of motoric improvement in speed of contralateral hand movement and finger dexterity at short-term follow-up. The extent of improvement was not predicted by preoperative medication responsiveness or age.

P838

Pseudobulbar crying spell during microelectrode recording of the GPi in a patient with Parkinson's disease

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Objective: To describe a single case of pseudobulbar crying during microelectrode recording of the GPi for Parkinson's Disease.

Background: There have been many reports of cognitive and mood changes associated with acute and chronic deep brain stimulation (DBS) of multiple brain targets. We have previously reported pseudobulbar laughter following thalamotomy, and pseudobulbar crying following subthalamic nucleus region DBS. Here we present a case of pseudobulbar crying associated with microelectrode recording for placement of a GPi DBS for PD. A 47-year-old woman with idiopathic PD undergoing GPi DBS was intra-operatively examined by a movement disorders neurologist and psychiatrist during microelectrode recording (Axon Systems) for placement of a DBS device. She had a previous history of mild treated depression (pre-operative Beck Depression Index-11) and was being treated with sertraline 75 mg/day.

Methods: Single case report

Results: An episode of pseudobulbar crying was documented during the first pass of microelectrode recording in the sensorimotor territory of the GPi. During the episode the patient reported that she was crying and she did not know why. She was questioned during and after the episode about her emotional state at the time of the crying spell and she stated she denied sadness. She had not experienced any similar spells previously. The crying spell lasted between 1 and 2 min and spontaneously resolved. It did not recur during or after the operative case.

Conclusion: Spontaneous crying spells in the operating theater during deep brain stimulation may represent pseudobulbar crying. The mechanisms for this response are unknown although both penetration of the frontal lobes as well as the GPe or GPi could be responsible for this response. A careful intra-operative examination may help differentiate an emotional crying spell from a pseudobulbar crying spell. The mechanisms for this response remain to be investigated as does the effect of the pre-morbid psychiatric status.

P839

Deep brain stimulation of the GPi treats restless legs syndrome associated with dystonia: Report of a case

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Objective: To describe a case of primary generalized dystonia with associated restless legs syndrome (RLS) in which the RLS resolved with GPi DBS.

Background: It has been reported previously that pallidotomy was effective at abolishing RLS contralateral to the lesion [Rye and Delong, 1999] in a patient with Parkinson's disease. This response has not been documented in dystonia or with GPi DBS.

Case Report: A 26-year-old woman with primary generalized dystonia since childhood underwent staged, bilateral GPi DBS. Prior to the surgery, she felt an uncomfortable sensation on both of her legs with a "need to move them". She often acted on this need to move her legs. She had no tremor in either leg but did have severe dystonia of her voice, arms, trunk, and legs; and had a dromedary gait.

After the right DBS lead was placed, her dystonia, especially on the contralateral side, improved significantly. Along with this, the uncomfortable sensation and need to move resolved in the left leg. Following the left GPi DBS, the sensation and need to move resolved in the right leg. Subsequently, approximately 7 months later the left GPi DBS had to be removed secondary to infection. The RLS symptoms returned in her right leg only, and resolved 3 months after reimplantation of the GPi DBS.

Conclusion: GPi DBS may be effective at controlling RLS in the setting of dystonia. The "uncomfortable sensation" and the "urge to move" her legs in this report clearly distinguish RLS symptoms from dystonic spasms or painful dystonia that may also improve with DBS. The mechanisms for the improvements in RLS symptoms both with DBS and with pallidotomy remain unknown.

P840

Rapid reappearence of tremor after discontinuation of subthalamic deep brain stimulation in Parkinson's disease: Evidence for a direct neuro-transmission interference

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Objective: To quantify the time course of tremor amplitude and frequency after discontinuation of subthalamic nucleus (STN) deep brain stimulation (DBS) in Parkinson's disease (PD), using a computerized 3D ultrasound-based measuring method combined with surface electromyography of different forearm muscles.

Background: Clinically, after discontinuation of STN-DBS a sequential pattern of the return of parkinsonian cardinal signs with a fast reappearence

of tremor can be observed. This led to the hypothesis, that STN-DBS may act by different mechanisms on the cardinal symptoms of PD.

Methods: Seven patients (mean age 67.1 ± 4.6 years) suffering from idiopathic PD were evaluated in medication off state 4–14 months after initiation of bilateral STN-DBS. Tremor amplitude and frequency of the more affected arm were measured at baseline and at 0.5, 1, 2, 3, 4, 5, 10, 15, 20, 25 and 30 min after discontinuation of STN-DBS. In addition, after switching DBS off and on, mean latency of re- and disappearence of tremor was determined.

Results: After discontinuation of STN-DBS, tremor rapidly reappears with a mean latency of 7.1 seconds (s) ± 1.2 s SE. Disappearence of tremor after switching DBS on was even faster at a mean latency of 3.7 s ± 1.1 s SE. In three patients, a significant change of tremor frequency within two seconds after switching DBS on could be detected. Tremor amplitude quickly increased after discontinuation of STN-DBS, reaching a maximum amplitude after 2 min (29.6 mm ± 8.1 mm SE, compared to baseline 1.8 mm ± 0.8 mm). Subsequently, tremor amplitude gradually decreased to a mean level of 22.4 mm ± 7.1 mm SE 10 min after switching STN-DBS off and remained stable during the following 20 min of DBS discontinuation.

Conclusion: After discontinuation of STN-DBS in PD, tremor reappeared rapidly within seconds, reaching a maximum amplitude after 2–3 min of discontinuation, and in some patients STN-DBS almost immediately changed tremor frequency. These findings support the hypothesis, that DBS acts by direct interference with neuro-transmission of the basal ganglia loops involved in tremor.

P841

An audit of the incidence and types of epilepsy occurring after deep brain stimulation for dystonia

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Objective: 1) To document the frequency and types of seizures occurring in the dystonia population that underwent deep brain stimulation (DBS) at Charing Cross Hospital between 1998 and 2003 and 2) To compare this data with that obtained from the PD population who underwent DBS in this institute during the same period.

Background: DBS is a potential treatment for various forms of medically refractory primary dystonia. The preferred surgical target for dystonia is the Globus Pallidus internus (GPi). Our review of the published literature on GPi stimulation for dystonia showed that none of 73 published dystonia cases developed a seizure after surgery. However, one patient experienced deja vu phenomena whilst stimulation was 'on' because of a misplaced electrode in the temporal lobe.

Methods: The case records of *all* the dystonia and PD patients who had undergone DBS at Charing Cross Hospital during the above epoch were inspected for the presence and details of a seizure disorder both pre- and post-operatively. This data was then documented on a standard proforma along with the stimulation parameters. The incidence of a seizure disorder arising after surgery was compared for PD versus dystonia using Fisher's exact test.

Results: There were 16 dystonic patients (12F, 4M), mean age 36.3 years (range: 22–50), all of whom underwent bilateral GPi stimulation (one had a previous pallidotomy). Ten had generalised dystonia, 5 spasmodic torticollis and 1 myoclonic dystonia and their bipolar stimulation parameters (mean ± ranges) were: 4.8 V (0–7.0), 131.6 Hz (0–180), 172.5 μsec (0–240). Two dystonic patients (12.5%) were noted to have had seizures preoperatively whilst 4 patients (25%) developed a seizure disorder after GPi electrode implantation; 5 had generalised dystonia and 1 myoclonic dystonia. The post-operative seizures began a mean of 9.75 months (range: 3–24) after surgery and included generalised tonic-clonic seizures (1 case) and partial complex seizures (3 cases).

In contrast of 21 PD patients (6 F, 15 M) who underwent DBS only one had a seizure disorder, which was present both pre- and post-operatively. For the PD patients the DBS procedures were: 10 bilateral and 9 unilateral subthalamic (STN) stimulations (2 after thalamotomies, 2 after subthalamotomy and 1 after pallidotomy), 1 thalamic stimulation, and 1 GPi stimulation after contralateral pallidotomy. Not one of the PD patients developed a seizure disorder after surgery. The stimulation parameters for the PD group were: 4.2 V (1.5–5.7), 139 Hz (130–180), 105 μsec (60–180). Comparison between the 2 groups showed a significantly greater incidence of seizure disorders arising in the dystonic compared to PD patients after DBS ($P = 0.028$).

Conclusion: Our data indicates, in contrast to published literature, that for dystonic patients there is a 25% risk of a seizure disorder developing after bilateral GPi stimulation; a significantly greater risk than that for PD patients undergoing DBS. This information is important for pre-operative counselling of dystonia patients and is valuable to driving license authorities deliberating on the capacity of dystonic patients to drive after DBS.

P842

Different improvement of signs of Parkinson's disease after 1 year of subthalamic stimulation

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Objective: To study the Subthalamic (STN) stimulation effect on different signs (tremor, rigidity, akinesia and gait) of Parkinson's disease (PD), on a 1-year (Y) follow-up evaluation after the implant of electrodes.

Background: Hyperactivity of the STN may be the more important pathophysiological mechanism, underlying the motor complications observed in the advanced PD. Bilateral deep brain stimulation (DBS) of STN has been shown to improve parkinsonian motor symptoms but not all in the same degree.

Methods: Twenty patients (mean age: 54.4 years; disease duration: 11.3 years), underwent microelectrode recording-guided bilateral STN electrode implants. Patients were evaluated after 1 Y of monopolar DBS at 130 Hz, 60–90 μsec of pulse-width. The stimulus intensity ranged from 2.3–3.5 V. The Unified PD Rating Scale (UPDRS) was used to assess patients before and after surgery; we considered the part III (motor examination) as total score (item 18–31; range: 0–108) and separately the items for specific signs: tremor (21–22; range: 0–28), rigidity (22; range 0–20), akinesia (23–26; range 0–40) and gait (29: range: 0–4)

Results: After 1 Y total motor score in the Drug(D)-off/Stim(S)-on condition was 30.3; compared to pre-operatory D-off state (59.6), was improved by 49.2%. Tremor score improved by 69.3%; rigidity decreased by 52.6%; akinesia improved by 40.9% and gait by 30.6%. All these changes were significant at the statistical analysis ($P < 0.001$). Levodopa administration (D-on/S-on condition) did not affect significantly total motor examination (58.3%) and scores for tremor and rigidity (respectively 78.5% and 65.8%). A significant ($P < 0.01$) amelioration was observed on akinesia (54.3%) and gait (44.8%).

Conclusion: Bilateral STN-DBS produce a strong improvement of the total motor examination in the Off state, more evident for tremor and rigidity (>50%) and less impressive for akinesia and gait (<50%). This trend may be due to the more important influence of other systems outside of the basal ganglia on akinesia and gait control, as compared to tremor and rigidity. The additive effect of levodopa may support the role, in PD, of the dopaminergic denervation in the frontal and motor cortex. Nevertheless the presence of an incomplete symptomatic effect with the combined treatment (D-on/S-on), mainly on akinesia and gait, confirm the existence of non-dopaminergic lesions in PD.

P843

Only physical aspects of quality of life are significantly improved by bilateral subthalamic stimulation in Parkinson's disease

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Objective: To investigate by patient's self assessment the influence of high frequency chronic deep brain stimulation of the subthalamic nucleus (STN DBS) on physical versus mental aspects of quality of life (QoL) in Parkinson's disease (PD).

Background: The well known global improvement of QoL after STN DBS in PD appears contradictory with the behavioral disturbances often observed postoperatively. Indeed the respective impact of DBS on physical versus mental aspects of QoL in PD remains unknown.

Methods: The results of 30 patients for the Unified Parkinson's disease Rating Scale (UPDRS) and Parkinson's disease Questionnaire 39 (PDQ39) were compared preoperatively and after 12 months of STN DBS.

Results: When off dopa condition was compared preoperatively versus 12 months postoperatively, UPDRS part II and part III were significantly improved with respectively 43.2% and 53.2%. UPDRS part I remained no significantly improved (10.9%) at 12 months. In PDQ39, the global score was significantly improved after surgery (22.8%). Four subscores were significantly improved: mobility (25.5%), activity of daily living (39.7%), stigma (40.8%) and bodily discomfort (33.6%). Three subscores however remained no significantly improved: emotional well being (9.4%), social support (1.8%) and cognition (11.2%) ; and one was no significantly impaired: communication (− 4.1%).

Conclusion: From clinician's point of view, STN DBS is very effective, regarding the UPDRS part II and III improvement. From patient's point of view however, the physical aspects of QoL are clearly improved, without significant improvement of the mental ones, regarding the PDQ39 subscores and the UPDRS part I. These results confirm the beneficial effect of STN DBS on the motor aspects of PD without significant influence on the non motor ones.

P844

Chronic bilateral subthalamic nucleus stimulation in advanced Parkinson's disease: Computerized gait analysis at 3 months and at 1 year postoperatively

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Objective: To study prospectively the long term-term effects of chronic bilateral subthalamic nucleus (STN) stimulation on gait in patients with advanced idiopathic Parkinson's disease and to compare its effect to medication with levodopa using computerized gait analysis.

Methods: Eight patients with advanced Parkinson's disease (3 women, 5 men, mean age 68.5 ys) underwent bilateral STN-stimulation. The preoperative and postoperative (3 and 12 months after surgery) spatial and temporal gait parameters were analyzed in off-drug and on-drug conditions. Instrumental gait analysis was performed using a computer-assisted gait analyzing system (Ultraflex, Infotronic, The Netherlands).

Results: In the medication "off" condition, objective gait scores were improved with bilateral STN-stimulation both at 3-month and 12-month follow-up. Preoperative gait measurements during best medication "on" states were also improved with bilateral STN-stimulation as demonstrated in the follow-up assessments. Net medication effects at 3 and 12 months postoperatively were equivalent to net stimulation effects.

Conclusion: Bilateral STN-stimulation resulted in a substantial improvement of gait parameters in our cohort of elderly patients with advanced Parkinson's disease. Net medication effects were equivalent to net stimulation effects, but the combination of both led to further improvement.

P845

Acute effects of L-DOPA and subthalamic stimulation on depression and hedonic tone in Parkinson's disease

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Background: Deep brain stimulation (DBS) of the subthalamic nucleus (STN) in Parkinson's disease (PD) may influence not only the motor symptoms of the disease, as the basal ganglia also contribute to cognitive and emotional processes.

Objective: To evaluate acute changes in hedonic tone and mood caused by STN DBS in comparison/addition to L-DOPA.

Methods: Effects of bilateral electric stimulation of the STN and L-DOPA exposure were investigated in 15 patients with PD. Before and 3 months after STN DBS operation symptoms of depression and anhedonia were rated in the off and on stimulation and in the off and on medication condition, using the Beck Depression Inventory (BDI) and the Snaith-Hamilton Pleasure Scale (SHAPS).

Results: Analysis of the BDI total scores using the 'General Linear Model' with repeated measurements revealed significant effects of the within-subjects-factors medication and stimulation (medication: $F = 27.3$, $P < 0.001$; stimulation: $F = 12.0$, $P < 0.001$) indicating a positive effect on depression after both STN stimulation and L-DOPA. Concerning the SHAPS total scores test of within-subjects effects demonstrated a significant main effect of the medication ($F = 5{,}18$, $P = 0.039$), but no main effect of the stimulation. Hedonic tone therefore was improved by L-DOPA but not by STN-simulation.

Conclusion: First these results demonstrate a single dissociation of depressive symptoms and anhedonia at the level of the basal ganglia. Second a postoperative reduction of dopaminergic medication can explain decreased hedonic tone in PD patients treated with chronic STN DBS.

P846

Fear recognition is impaired by subthalamic nucleus stimulation in Parkinson's disease

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Objective: To study emotional recognition in Parkinson's disease (PD) patients with chronic high frequency deep brain stimulation of the subthalamic nucleus (STN DBS).

Background: Behavioral disturbances such disorders of mood, apathy or indifference are often observed in PD patients with STN DBS. Neuropsychological modifications causing these adverse events induced by STN DBS remain unknown, even if limbic disturbances are hypothesized.

Methods: Twelve PD patients were prospectively assessed 3 months before and 3 months after STN DBS using a computerized paradigm of recognition of emotional facial expressions [Ekman and Friesen, 1976]. Two different series of 55 pictures of facial expressions were presented respectively before and after surgery. Patients had to classify the pictures according to 6 basic emotions (fear, sadness, disgust, anger, happiness and surprise). The intact ability to percept faces was firstly assured using the Benton Recognition Test. Statistical analysis was performed using the non parametric Wilcoxon test for paired comparison.

Results: None of the patients were impaired in face recognition assessment by the Benton Recognition Test, both in pre and post operative situations. Recognition of fear expressions was significantly and selectively reduced 3 months after stimulation was turned on (80% fear expressions recognized before vs. 30% after surgery, i.e., 63% of reduction).

Conclusion: Our results demonstrate prospectively for the first time a selective reduction of recognition of facial expressions of fear by STN DBS. This impairment could be the first neuropsychological marker of a more general limbic dysfunction, thought to be responsible for the behavioral disorders reported after STN DBS.

P847

On demand deep brain stimulation for essential tremor: An approach to avoid tolerance?

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Background: Deep Brain Stimulation (DBS) of the thalamic nucleus ventralis intermedius (VIM) is an established therapy for essential Tremor (ET), but loss of efficacy due to tolerance may occur (2).

Objective: To evaluate if On Demand DBS of the VIM can avoid tolerance.

Methods: Among 18 patients who obtained DBS were 3 patients with ET who in the past 2 years obtained left hemisphere DBS implants targeting the VIM. These patients were instructed to switch on DBS only when using their right hand for motor tasks (e.g., writing, drinking, eating). DBS programming was chosen that allowed the best functional improvement with no side effects. In the follow-up, only stimulation amplitude was increased if necessary. Tremor was evaluated by the Clinical Rating Scale for Tremor (CRST).

Results: After DBS implantation 2 patients had a lesioning effect for a few days. Thereafter in all patients DBS led to tremor suppression of the

right arm when stimulation was switched on and tremor returned to preoperative state if DBS was discontinued [tremor of right arm (item no. 5 of CRST) presurgery: 4.7 ± 1.2/1 year postsurgery DBS-ON: 0.3 ± 0.6 and DBS-OFF: 4.6 ± 1.5]. Patients had DBS switched on around 30% of the day. Stimulation amplitude had to be increased from 1.5 ± 0.5 volts to 1.7 ± 0.6 volts in the first months and remained stable for the follow-up. Functional disability, rated by the score of activities of daily living of the CRST, improved from 13.7 ± 3.5 preoperatively to 0.3 ± 0.6 1 year after surgery.

Conclusion: 1.) Compared to the literature (1, 2) where patients switched off DBS only at night, our patients needed a smaller increase of stimulation amplitude over time (see diagram). This, and the use of DBS only 30% of the day, leads to a significant prolongation of battery lifetime, which makes On Demand DBS a consideration for some ET patients with DBS. 2.) In our small number of patients no tolerance phenomena (e.g., secondary therapy failure, tremorrebound) occurred. To further support the advantages of On Demand DBS, a clinical trial with a larger number of patients is needed.

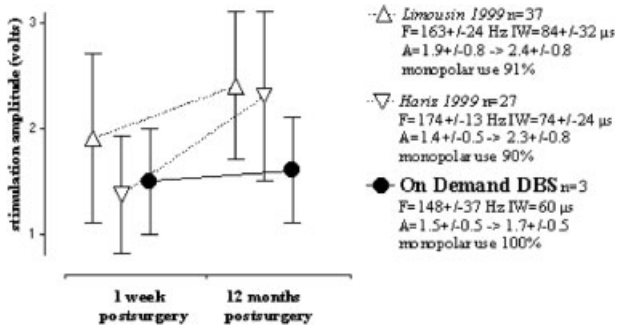

FIG. 1 (P847). Stimulation amplitudes in the follow-up as compared with the literature.

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P848

Pallidal neuronal activity in generalized dystonia

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Objective: To characterize spontaneous neuronal activity in internal (GPi) and external globus pallidus (GPe) in patients with generalized dystonia undergoing deep brain stimulation.

Background: The current model of basal ganglia disorders relates dystonia and other hyperkinesias to a hypoactive basal ganglia output. Other potential mechanisms include abnormal patterning of neuronal discharges or abnormal "focussing" of basal ganglia activity.

Methods: Spontaneous multi-unit-activity (MUA) and local field potentials (LFP) were recorded in 11 patients with generalized dystonia undergoing bilateral implantation of electrodes for deep brain stimulation. Surgery was performed under general anesthesia with propofol/remifentanyl (PA). Recordings were performed with tungsten microelectrodes (FHC, USA) in a Ben-Gun-arrangement (n = 9) or along multiple subsequent trajectories using a single tetrode (TREC, Germany). Single unit activity (SUA) was isolated "off-line" using a template-matching based algorithm (Spike2, CED, UK) or a cluster-analysis for tetrode recordings [Spiker by Rebrik et al.]. SUA was characterized by calculating mean firing rate, burst index, interspike interval histograms (IHI), autocorrelation and crosscorrelation of simultaneously recorded units. Based on typical IHI shapes(1) the firing pattern of cells was characterized as bursting, burst-like multimodal, burst-like skewed, tonic or irregular.

Results: Eighty-eight units in GPe and 180 units in GPi were characterized. Results are summarized in table 1. GPe and GPi did not differ significantly (χ^2 test, $P = 0.22$) in discharge behavior or mean firing rate, although a tendency was found towards more bursting type activity within GPe and more irregular or tonic activity within GPi.

Conclusion: We found remarkably similar neuronal discharge behavior within GPi and GPe of patients with severe generalized dystonia. Firing rates were overall reduced compared to patients with Parkinson's disease (PD) and only few cells within GPi displayed the typical tonic discharge pattern described in normal monkeys, primate models of PD, or recordings in PD patients. Our results are in agreement with the previous report of Vitek et al.(2) and suggest abnormal patterning of basal ganglia activity as a pathophysiological correlate of dystonia.

TABLE 1 (P848). *Neuronal discharge behavior in generalized dystonia*

	Discharge pattern	n	Rel. proportion (%)	Mean firing rate (mean ± SD)
GPe	bursting	3	3,4	19,9 ± 17,7
	burst like skewed	58	65,9	14,1 ± 10,6
	burst like multimodal	0	0	
	irregular	13	14,8	13,9 ± 13,1
	tonic	14	15,9	40,1 ± 30,9
	total	88	100	18,6 ± 18,4
GPi	bursting	10	5,6	22,2 ± 22,1
	burst like skewed	86	47,8	13,6 ± 9,6
	burst like multimodal	3	1,7	25,0 ± 8,7
	irregular	41	22,8	14,0 ± 10,0
	tonic	40	22,2	29,6 ± 16,8
	total	180	100	17,9 ± 14,0

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P849

Reversible catatonia/catalepsy and sub thalamic nucleus deep brain stimulation (STN DBS) in Parkinson's disease (PD)

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Objective: Characterize a new reversible behavioral and motor effect in a PD patient (pt) with STN DBS.

Background: Catatonia has been described as a complex syndrome which includes catalepsy in both psychiatric and medical disorders. Catalepsy has been defined by some authors as mutism, akinesia and posturing without evidence of a psychiatric disorder [e.g., Parkinson's Disease and Movement Disorders, 3rd edition, Eds. J. Jankovic, E. Tolosa, pp. 717–728]. We have recently observed reversible induction of a transient cataleptic-like state in a PD pt. during STN DBS adjustments. To our knowledge, catalepsy has not been described in any written publications for PD pts. either with or without STN DBS. A similar case may have been seen by others [Paul Bejjani, personal communication].

Methods: A 65 year old patient with medically intractable PD (UPDRS off Total/ III = 76/43, UPDRS on Total/III = 43/21) underwent bilateral STN DBS. He had no history of psychiatric illness or seizures. He was tested and videotaped pre-surgery and at 3-month intervals according to a modified CAPSIT protocol and videotaped during DBS adjustments.

Results: During intraoperative placement of DBS electrodes he had sensori-motor driven cells in STN and contralateral motor improvement. Three months after surgery he had bilateral improvement in bradykinesia, stiffness, and walking. He had lowered levodopa by 70% at stimulator settings of R IPG C+ 0−, 2.2 V, 60 µs, 130 Hz, L IPG C+ 1−, 2.0 V 60 µs 130 Hz. At 6 months, UPDRS off medicine/on stimulator score improved to 26. At 3 months, during a DBS adjustment, he had additional

motor improvements as the L IPG voltage was increased to 2.5 V. However, as frequency was increased from 130–150 Hz the patient had a cataleptic like spell. He became suddenly akinetic and mute. His arms remained in a fixed frozen active posture with one hand on his chest. He exhibited waxy flexibility when attempts were made to move his arms. His eyes remained open and were conjugately deviated left and upward without nystagmus. He could not follow commands. He could report accurately what he had heard during the episode. He said he tried to speak but could not. He said he could see but that everything was blurred. The episode lasted 5 min after the left stimulator was turned off. Since then, he has been observed to have either complete or partial spells (in which he could occasionally follow some commands) at contacts C+ 2−,1+ 2−, and 1+ 3−. All Contact impedances have been normal. His ability to speak usually returned within 5 min but he has not felt "normal" for up to 10 min. Some of these episodes occurred with a change in voltage of only 0.1 V. The latency for onset of the episodes ranged from 1 sec to 5 min. The episodes subsided more quickly if the stimulator voltage was reduced. He has exhibited no mannerisms or stereotypies. All these episodes have only occurred during DBS stimulator adjustments.

Conclusion: A reproducible, reversible cataleptic-like syndrome has been observed in a PD patient during STN DBS adjustments. Further studies may elucidate the anatomy and physiology of this effect. Videotapes will be presented.

P850

Bilateral stimulation of the subthalamic nucleus (STN) in Parkinson's disease (PD): A long-term follow up of non-surgical, non-reversible clinical complications in 117 patients

C. van der Linden, H. Colle (Belgium)

Objective: To determine the long-term non-surgical non-reversible complications in patients with PD, who underwent chronic stimulation of the STN.

Background: Bilateral STN stimulation in advanced PD has become a standard treatment in many centers across the world. There have been reports on irreversible changes of the clinical presentation after chronic STN stimulation, such as speech and behavioral disturbances. We reviewed the possible irriversible long-term complications in 117 PD patients who underwent chronic STN stimulation.

Methods: The data of 117 consecutive PD patients with pre-operative motor complications and dyskinesias who received bilateral STN stimulation in our center from 1998 until 2003 were reviewed. None of the patients had a psychiatric history, nor signs of dementia prior to surgery. Reversible STN stimulation-related and anti-PD related side effects, infections and hardware problems were excluded from analysis. The complications should not be present within 3 months after surgery and reviewed at least one year after surgery. The pre-op levodopa-equivalent daily dose (LEDD) was compared to the post-operative LEDD for each complication. Parts of the pre-operative UPDRS III scores were compared to the post-operative scores only at the best on before and after surgery where applicable. In all complications, adjustment of stimulation parameters or anti-PD medication should not lead to improvement.

Results: The mean interval between surgery and analysis was 3 (range 1–6) years. 27/117 (23%) patients (mean age 66 years and mean disease duration 12 years) had severe gait disturbances with frequent falls (pre-op vs. post-op UPDRS 28,29,30 was 3 and 5, respectively, and the mean pre vs. post-op LEDD was 1,229 and 918, resp); 11/117 (9.5%) patients (mean age 65 years and mean disease duration 13 years) had severe speech disturbances, including hypophonia or palilalia (pre-op vs. post-op UPDRS 18 was 0.8 and 2.8, respectively and the mean pre vs. post-op LEDD was 1,300 and 1,260, resp); 11/117 (9.5%) patients (mean age 69 years and mean disease duration 13 years) had dementia (MMSE scores below 24), 9 of whom had gait disturbances; 9/117 (7.5%) patients (mean age 52.6 years and mean disease duration 10.7 years) had evidence of hypomania, 8 of whom were men (mean pre vs. post-op LEDD was 1,175 and 605, respectively); 4/117 (3.4%) patients (mean age 56 years and mean disease duration 18 years) had evidence of depression (as defined by DSM IV criteria). Their mean pre vs. post-op LEDD was 1,118 and 425, respectively.

Conclusion: Severe speech and gait disturbances are common in PD patients undergoing long-term chronic STN stimulation. Dementia is associated with gait disturbances and higher age, whereas hypomania is present in young men, with short disease duration, requiring low doses of anti-Parkinson medication. Depression is not common in our serie of patients undergoing chronic STN stimulation. A controlled study comparing operated to non-operated patients is necessary to determine whether the aforementioned complications are a direct result of chronic STN stimulation, the natural progression of Parkinson's disease or both.

P851

Unilateral deep-brain stimulation of the subthalamic nucleus (STN-DBS) in Parkinson's disease (PD): Correlation of clinical results with electrode position

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Objective: To correlate the clinical outcome with the anatomical localization of the active/s electrode in a group of advanced PD patients treated with chronical unilateral STN-DBS.

Background: Chronic unilateral electrical subthalamic nucleus deep brain stimulation (STN-DBS) produced a perceptible improvement, as was reported in our group of advanced PD patients [Mata, Stereotact Funct Neurosurg, 2001], and by few others authors [Kumar, Neurology, 1999; Van Blecom, Mov Disord, 2002; Arzbaecher, Neurology, 2003]. However, there is no reported information about electrode localization in unilateral STN-DBS. We investigated the correlation of localization of the active/s electrode with the clinical outcome in our group of advanced PD patients treated with chronical unilateral STN-DBS.

Methods: Nine advanced PP were implanted with unilateral quadripolar electrodes (Medtronic 3389) in the subthalamic nucleus. Operated side was selected according to the most affected hemibody. The patients were assessed pre- and postoperatively after 1, 3, and 6 months of follow-up. A postsurgical MRI-1,5T was used to localize the electrode. Stereotactic MRI images were superimposed to anatomic atlas (Schaltenbrandt-Wharen) using a specific software developed by the investigators (STEREONAUTA PLUS; Neuronautas S.L.). Cerebral coordinates were calculed in relation to the middle intercommisural point (MIP).

Results: UPDRS-III improved on average of 30% in OFF medication (6 months). All but one electrodes were on bipolar configuration. Based on experimental studies [Rank, Brain, 1975], current flow in bipolar configuration, is most likely to affect the fibers situated between the two poles, and parallely to the current flow. According to that, the actives electrodes in our patients were placed in: the dorsolateral zone of the STN and adjacent Zona Incerta (ZI) and Forel Fields (H1H2) in four patients; inside the STN in two patients; below the STN, between the fibers and Substantia Nigra (SN) in one patient; in the interface between the ZI, Internal Capsula (IC) and the upper border of the STN in one patient; and medial to the STN, between ZI and Nucleus Ruber (NR) in one patient.

Conclusion: Clinically effective electrodes in our patients were placed beetween STN and adjacent zones, as ZI, H1H2, and fibers sorrunding the STN. Pure nuclear stimulation seems not to be needed to achive a good clinical result.

P852

Effects of different parameter settings on the intelligibility of speech in patinets with Parkinson's disease treated with deep brain stimulation in the subthalamic nucleii

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Objective: To evaluate the effects of different electrical parameter settings on the intelligibility of the speech in patients with Parkinson's disease (PD) treated with bilateral Deep Brain Stimulation (DBS) in the Subthalamic nucleus (STN). This is a part of a larger study.

Methods: Ten patients treated with DBS for 15.0 ± 5 mth (mean, sd) with a significant motor symptom reduction (UPDRS III), were included. Nine of them had speech disturbances preoperatively. In random order, 11 DBS parameter settings were tested in medication off condition (25%

changes of amplitude and varied frequency). The patients read five nonsense sentences per setting. A listener panel (10 listeners) transcribed the nonsense sentences as perceived.

Results: With the patients normally used setting there was no significant group difference between DBS off and on, but in four patients the intelligibility deteriorated with DBS on. Increased amplitude or frequency caused significant impairments of intelligibility.

Conclusion: The amplitude and frequency of the DBS have a major influence on the verbal intelligibility. Meticulous parameter adjustments when programming DBS are important to minimize the side effect.

P853

Are complications less common in deep brain stimulation than in ablative procedures for movement disorders?

P. Blomstedt, M.I. Hariz (Umeå, Sweden; London, UK)

Objective: To compare side-effects and complications of deep brain stimulation (DBS) with those of ablative lesions, in functional neurosurgery for movement disorders.

Methods: All surgical procedures for movement disorders at our institution between 1990 and 2002 were analysed. 197 consecutive patients underwent a total of 256 procedures, of which 127 were stereotactic lesions (128 brain targets) and 129 DBS (151 implanted electrodes). Mean age of patients was 63 years for DBS and 65 years for lesion. In Parkinson's disease (PD) patients, 100 stereotactic lesions were performed, and in essential tremor (ET) patients, 27. For DBS the figures were 69 for PD and 49 for ET. Of the 127 lesion procedures, 76 were in the posteroventral pallidum (PVP) and 51 in the ventral intermediate (Vim) thalamus. Of the 129 DBS, 96 were in the Vim, 22 in the Subthalamic nucleus (STN) and 11 in the PVP.

Results: Within a minimum follow up of 6 months, 67.4% of DBS patients and 42.5% of leison patients experienced side-effects or complications. Surgical complications (seizures, hemorrhage, confusion etc.) did not differ between the two groups, whereas brain-target-specific complications showed differences between patients who had DBS and those who had lesions. There were complications in 70% of the patients who had Vim thalamotomy (dysarthria, gait and balance disturbances), in 57% of patients with unilateral Vim DBS, and in 75% of patients with bilateral Vim DBS, although most of these were reversible upon switching off (or altering) stimulation parameters. Following pallidotomy, there were 19% transient and 5% permanent side-effects (visual defects, dysarthria, dysphonia, dementia). Of the 12 bilateral staged pallidotomies, 25% had transient side-effects, and 5% permanent (dysarthria/dysphonia). Nine adverse effects were recorded for the 11 patients with pallidal DBS. Two of the pallidal DBS patients had transient dysarthria and one had a non-reversible dysphonia. In 12 patients with STN DBS, 15 side-effects, mostly psychiatric, were encountered. Six patients had confusion, changes of mood or cognitive decline, and three had dysphonia. Hardware-related complications occurred in 13.2% of the patients with DBS.

Conclusion: Ablative surgery does not harbour more perioperative complications than DBS. Some of the side-effects following lesions are reversible and most but not all DBS side-effects are reversible. In the Vim and probably in STN, DBS is safer than lesioning, while in the pallidum, unilateral lesions are well tolerated.

P854

The role of the surgical movement disorder nurse specialist

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Objective: To publish a document that could be used nationally to ensure appropriate specialist nursing care for patients undergoing functional neurosurgical procedures for movement disorders.

Background: Surgery for movement disorders is becoming increasingly common, not only in the UK, but also internationally. There is clearly a need for nurses to develop expertise in this field of neuroscience nursing in order that patients receive appropriate care delivered by skilled practitioners.

This is a relatively young specialty within nursing. The first nurse to be appointed in England specifically to manage the care of patients in surgical neurology came into post in 1996, when most patients were undergoing lesional procedures for Parkinson's disease and tremor. Since that time, surgical techniques have advanced and most patients for whom such surgery is appropriate are now treated by implantation of deep brain stimulators. The range of movement disorders treated has also increased to include disorders such as dystonia, chorea and other more unusual conditions. There are currently many areas of research in this field that will almost certainly change the way these conditions are managed in the future. The numbers of patients who have implanted neurostimulation devices is growing and Surgical Movement Disorder Nurse Specialists in the UK have become central to the care of this client group, becoming increasingly involved directly in the management of neurostimulation devices and titration of these alongside adjustment to the patient's medication.

Methods: A steering group was set up to undertake this project and to secure funding for the publication of the document.

Conclusion: This publication has been produced with the support of the Royal College of Nursing of the United Kingdom and the Parkinson's Disease Nurse Specialist Association (PDNSA). It was funded by contributions from the National Tremor Foundation, the Dystonia Society, the Multiple Sclerosis Society and the PDNSA. It is seen as an important step in ensuring that the role of the Surgical Movement Disorder Nurse Specialist develops appropriately and consistently to meet the needs of this client group. By clearly defining the role, it will allow nurses and their managers to set standards of practice and identify areas for further training and development.

P855

Gpi DBS has only moderate benefit for mixed involuntary movements after thalamic stroke

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Objective: To report a patient with mixed involuntary movement disorder after lateral thalamic stroke who underwent surgical therapy with globus pallidus interna (Gpi) deep brain stimulation surgery (DBS).

Background: Ablative surgery is commonly done for Parkinson's disease, Dystonia and Essential tremor but its efficacy is unknown in patients with involuntary movements after stroke affecting the basal ganglia or thalamus. Mixed involuntary movements are a rare, but well described entity in patients after lateral thalamic stroke and often are particularly resistant to current medical therapy.

Methods: Case report on a 63-year-old female with a history of atrial fibrillation and right ventrolateral thalamic stroke 2 years prior to surgical intervention. The mixed involuntary movements, which affected the left sided extremities, began several days after the stroke, which initially presented with moderate left sided weakness. The weakness recovered significantly, but involuntary movements worsened. In addition her trunk and jaw started showing involuntary movements. The patient had mild left sided hemiparesis, left sided loss of joint position sense, hemiataxia, a predominantly action and postural tremor, hemichorea, ankle dyskinesia, irregular dystonic tremor and myoclonic jerks of the hand on the left side. In addition she also had trunkal dyskinesia and involuntary opening and closing of the jaw. Her gait was severely affected by involuntary movements. Medical treatment including neuroleptics, benzodiazepines, anticholinergic, dopaminergic agents, neurontin and botulinum toxin A all failed to improve the patient's symptoms.

Results: Intra-operatively globus pallidus externa (Gpe) and Gpi activity was recorded. Gpe single unit activity was lower in frequency than Gpi. No single units were found in either nucleus. With a lower impedance electrode, Gpi consisted of moderate to high amplitude multi units. Ankle kinesthetic activity was located in two separate areas in the Gpi. Intraoperative stimulation testing demonstrated no adverse optic or motor responses to 4.0 volts. Importantly, right-sided Gpi-DBS produced moderate improvement in involuntary movements on the left lower extremity, but no change occurred in the left hand, jaw or trunk.

Conclusion: Gpi DBS has moderate benefit in patients with mixed involuntary movements after lateral thalamic stroke. Our patient had mod-

erate improvement in lower extremity chorea and ankle dyskinesia, but no benefit in upper extremity, trunk and jaw involuntary movements. Intraoperative recordings indicated location of the electrode in the Gpi in leg sensory-motor area, which might explain partly the lower extremity improvement only. The suboptimal response to Gpi DBS might be also due to the complex character of movement disorders observed in this patients population. Other targets such as Vim or STN alone or in combination with Gpi might be explored in control of this rare and medically intractable condition.

P856

Long-term changes of subthalamic nucleus (STN) deep brain stimulation (DBS) parameters in PD patients

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Objective: STN DBS has shown significant improvement in all cardinal symptoms of PD. It has been particularly useful in a subset of advanced younger onset PD patients. However, a long-term efficacy and, especially, long-term changes in parameters of stimulation need to be elucidated.

Methods: We have followed prospectively all patients who underwent bilateral STN implantation in our center. Included are consequent patients with idiopathic PD without prior brain surgeries. We have followed UPDRS motor scores, medication usage and following stimulation parameters: voltage, impedance, frequency, pulse-width and total current output. As it takes a few months for stimulation parameters to stabilize after DBS implantation, we arbitrarily used 6 months post implantation parameters as a baseline for long-term follow-up.

Results: Thirty subsequent patients were followed at 6 months, 12 months, 36 months and 48–60 months post STN DBS implantation. The average "ON" motor UPDRS scores changed significantly ($P < 0.006$), but were still in the low range (6 vs. 11) from 6 months to the longest, 48–60 months follow-up; without significant changes in L-DOPA usage (532 vs. 567mg). The stimulation parameters changed, but only the rate and impedance on the left side were significantly higher ($P < 0.01$). Other stimulation parameters were also higher after five years, but did not show statistical significance. The voltage increased by 5%; frequency by 10%, pulse width by 12%, impedance by 16% and current output increased by 30%.

Conclusion: We observed relatively stable clinical motor outcome in 48–60 months follow-up of bilateral STN DBS in PD patients. There were minor increases in stimulation parameters necessary to control motor symptoms of PD. The overall current output however increased significantly as a net result of different stimulation parameter changes. Our findings suggest that long term STN DBS is continually efficacious, and at least in this 4–5 year follow-up the stimulation parameters are far from reaching pulse generator stimulation ceiling.

P857

Neuropsychological outcome of bilateral pallidal stimulation in dystonia

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Objective: To evaluate the effects of deep brain stimulation (DBS) of the globus pallidus internus (GPi) in dystonia on cognition, mood, functional ability and quality of life.

Background: GPi-DBS is a promising neurosurgical treatment for patients with different types of dystonia, but little is known about its neuropsychological effects. In Parkinson's disease (PD) GPi-DBS seems to be safe regarding cognition, however, some studies report post-operative impairments of executive functions and memory.

Patients and Methods: Twelve patients suffering from primary and secondary dystonia were assessed preoperatively and 3–12 months after bilateral implantation of GPi electrodes while on stimulation. The following tests were used: *Cognitive screening:* Mattis Dementia Rating Scale (Mattis); *Learning and Memory:* Rey Auditory Verbal Learning Test (RAVLT), Digit Span (WMS-R); *Phasic and tonic Alertness:* simple and precued visual reaction task (TAP); *Executive functions:* Phonemic and Category Word Fluency, Trail Making Test (TMT), Stroop Test; *Mood:* Beck Depression Inventory (BDI), Montgomery and Asberg Depression Rating Scale (MADRS); *Anxiety:* Beck Anxiety Inventory (BAI); *Hedonism:* Snaith-Hamilton-Pleasure-Scale (SHAPS); *Psychiatric Screening:* Brief Psychiatric Rating Scale (BPRS); *Quality of life:* modified PDQ 39; *Motor function:* Burke–Fahn-Marsden-Dystonia Rating Scale and Disability score.

Results: GPi-DBS significantly improved motor scores of the Burke-Fahn-Marsden-Dystonia Rating Scale by approximately 65% ($P < 0.01$). Furthermore, ameliorations were found postoperatively for quality of life (PDQ, $P < 0.01$) and mood (MADRS, $P = 0.02$, BDI, $P =$ 0,08) and trends for improved overall neuropsychiatric state (BPRS, $P = 0.06$) and diminished anxiety (BAI, $P = 0.05$). No changes were found in hedonism (SHAPS, $P = 0.12$). No significant effect of stimulation was observed on any of the cognitive tests: Mattis ($P = 0.12$), RAVLT: immediate recall ($P = 0.43$), recall after interference ($P =$ 0.79), delayed recall ($P = 0.76$), recognition ($P = 0.73$), Digit Span ($P = 1.00$), simple ($P = 0.16$) and precued ($P = 0.62$) visual reaction task, Phonemic ($P = 0.97$) and Category ($P = 0.28$) Word Fluency, TMT: part A ($P = 0.12$), part B ($P = 0.44$), B-A ($P = 0.78$), Stroop: conditions word ($P = 0.18$), colour ($P = 0.44$), and interference ($P =$ 0.48).

Conclusion: The present study confirms the efficiency of GPi-DBS for the treatment of dystonia resulting in significant improvement of motor functions and quality of life. Extending current knowledge, our data provide evidence that GPi-DBS might improve mood as well as anxiety and can be considered a safe neurosurgical treatment of dystonia with regard to cognitive functions.

P858

Intraoperative MR-imaging to confirm DBS lead placement prior to fixation

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Objective: To develop a new method of confirming the placement of deep brain stimulation (DBS) leads prior to removal of the stylet and fixation of the lead.

Background: The most widely used means of confirming DBS lead placement is through the use of intraoperative microrecording and macrostimulation, and occasionally fluoroscopy. These methods are usually successful in achieving accurate placement of DBS leads, but there are many patients in which the lead could have been placed in a more optimal location, thus increasing the therapeutic potential. Final placement is determined by a postoperative MR-imaging, but discovering that the lead is misplaced at this stage requires removal of the lead and a repeat surgery.

Methods: Image-Guided Neurologics (IGN) has developed an MR-compatible lead guide and remote introducer which are mounted directly to the skull. We are able to use a standard Leksell stereotactic frame and arc, but pass the lead through the IGN guide. Once the surgeon is satisfied with the placement through conventional means, the lead (with stylet left in place) is fixed with the lead guide and remote introducer, and the arc is removed. The patient is then imaged in a Siemens 1.5-T Sonata scanner. Previous safety studies have demonstrated that there is insignificant heating of the lead in this configuration ($<1°C$).

Results: If the lead is not optimally placed based on intraoperative MR imaging, it can be moved in the Z-plane by using the remote introducer, or removed and reinserted 3 mm in the direction of the X- or Y-plane. Once imaging shows that the lead is in the correct place, the stylet is then removed, the lead fixed, and the wound closed as usual.

Conclusion: Intraoperative MR-imaging of DBS leads is a reliable way to confirm lead placement prior to fixation and stylet removal, allowing immediate revision of lead placement as necessary.

P859

Impact on mood of subthalamic nucleus stimulation in patients with Parkinson disease

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Objective: To investigate the effect of bilateral deep brain stimulation in the subthalamic nucleus (STN-DBS) on mood change before and after one month and six months of operation in patient with advanced Parkinson disease (PD) using Hamilton Depression Rating Scale (HDRS) and Young's Mania Rating Scale (MRS).

Background: STN-DBS is a highly effective surgical treatment in patients with advanced PD. Neuropsychiatric changes such as mood change associated with STN-DBS has been previously reported.

Methods: Ten PD patients without history of psychiatric disorder received bilateral STN-DBS. Motor performance, behavioral dysfunction and mood were evaluated up to 6 months based on HDRS and MRS. The data was analysed using nonparametric tests (Kruskal-Wallis and Wilcoxon).

Result: Motor impairment was significantly improved at one month and six months follow-up. The differences among scores of HDRS and MRS before and after 1 month and 6 months of surgery were highly significant ($P < 0.05$, respectively, Kruskal-Wallis test). There was a significant decrease in HDRS after one month and six months of surgery ($P < 0.01$, respectively). On the other hand, there is significant increase in MRS after one month and six month of surgery ($P < 0.01$, $P < 0.05$, respectively). Seven patients didn't show significant change in MRS, while 3 patients show significant change in MRS.

Conclusion: These results indicate that STN-DBS may have some effect on mood as found in previous studies. Some depressive PD patients could benefit from STN-DBS, but there appears to be a subgroup of patients whose mood become hypomanic after STN-DBS. A longer follow-up study is needed to confirm this.

P860

One year follow-up of a randomized multicenter trial comparing unilateral pallidotomy and bilateral subthalamic nucleus stimulation in Parkinson's disease

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Objectives: 1) To compare the efficacy of bilateral subthalamic nucleus (STN) stimulation and unilateral pallidotomy in Parkinson's disease (PD) after one year follow-up of a randomized observer-blind multi center trial, and 2) To compare the results of this trial at the six months[1] and one year follow-up.

Background: Patients with advanced PD often suffer from response fluctuations and dyskinesias refractory to pharmacological treatment. Unilateral pallidotomy and bilateral STN stimulation can both improve PD symptoms in the off phase and dyskinesias in the on phase. We did the first randomized trial that directly compared unilateral pallidotomy and bilateral STN stimulation. At six months follow-up the results of this trial demonstrate that bilateral STN stimulation is more effective than unilateral pallidotomy in reducing parkinsonian symptoms in off and on phases. Dyskinesias duration improved more in the STN group, medication could be reduced more in the STN group, and the number of adverse effects was approximately the same for both operations.[1]

Methods: Thirty-four patients with advanced Parkinson's disease were randomly assigned to have unilateral pallidotomy or bilateral STN stimulation. Outcome measures were the change from baseline to one year in the motor part of the Unified Parkinson's Disease Rating Scale (UPDRS 3) in the off phase and on phase, dyskinesias (Clinical Dyskinesia Rating Scale and UPDRS 4), functional status (UPDRS 2 and Schwab and England scale), Parkinson's Disease Quality of Life questionnaire, changes in drug treatment, and adverse effects.

Results: After 1-year follow-up off phase UPDRS 3 score improved from 46.5 to 32 points in the group of pallidotomy patients and from 51.5 to 24 in the STN stimulation patients ($P = 0.002$). The on phase UPDRS 3 and the off phase Schwab and England functional scale improved significantly in favor of the STN stimulation patients. Antiparkinsonian drug reduction was greater in the STN group although the difference between the treatment groups was not significant. Dyskinesias severity and quality of life improved substantially in both treatment groups. One patient in each group had a major adverse effect. Moderate and mild adverse effects were approximately the same for both operations.

Conclusion: We found a greater efficacy of bilateral STN stimulation compared to unilateral pallidotomy for advanced PD after 1-year follow-up in this first randomized trial. The off phase functional status at 1-year follow-up was significantly different in favor of the STN stimulation group compared to the pallidotomy group, whereas this difference was not significant at 6 months follow-up. This suggests that the benefit of STN stimulation compared to pallidotomy is increasing over time.

P861

Subthalamic nucleus deep brain stimulation restores afferent inhibition in Parkinson's disease

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Objective: To investigate whether subthalamic nucleus deep brain stimulation (STN-DBS) can reverse deficient afferent inhibition in Parkinson's disease (PD).

Background: Peripheral sensory stimulation of the median nerve at wrist inhibits the response to transcranial magnetic stimulation (TMS) of the motor cortex at interstimulus intervals (ISIs) of about 20 msec (short latency afferent inhibition; SAI) and at ISIs of 100–600 msec (long latency afferent inhibition; LAI). We previously found that in PD patients SAI was impaired while on dopaminergic medications and may be related to the side effects of dopaminergic drugs such as dyskinesia. LAI was reduced both on and off medications and may represent a non-dopaminergic manifestation of PD [Brain 2003;126:1883–1894]. STN-DBS is increasingly being used to treat advanced PD and reduces dyskinesia. It is not clear whether the reduction in dyskinesia is entirely due to a decreased use of dopaminergic drugs or whether STN-DBS has direct effects on dyskinesia. Although the response to dopaminergic drugs strongly correlates with the effects of STN-DBS, it is unclear whether STN-DBS can also influence non-dopaminergic manifestations of PD.

Methods: We studied SAI and LAI in 7 PD-patients with bilateral STN-DBS off followed by on medications and with the stimulator switched on and off in random order (Med off-Stim off, Med off-Stim on, Med on-Stim off, Med on-Stim on). These results were compared to the findings in 7 age-matched controls. Median nerve stimulation was applied at the N20 somatosensory evoked potential latency plus 3 msec for SAI and at 200 msec for LAI before TMS to the contralateral motor cortex. The motor evoked potentials were recorded from the relaxed first dorsal interosseous muscle.

Results: SAI was normal in the Med off-Stim on and the Med off-Stim off conditions. The Med on-Stim off condition showed reduced SAI and this deficiency was normalized in the Med on-Stim on condition. LAI was equally reduced in PD patients in the Med off-Stim off and the Med on-Stim off conditions. Switching the stimulator on in the Med off-Stim on conditions partially reversed this abnormality while turning the stimulator on in the Med on-Stim on condition completely reversed this abnormality.

Conclusion: The results confirm our previous findings of impaired SAI in PD patients on medication and impaired LAI independent of the medications status. Restoration of SAI with STN-DBS in patients on medication suggests that it may have a direct ameliorating effect on the side effects of dopaminergic drugs such as dyskinesia. Restoration of LAI with STN-DBS raises the possibility that it may positively influence non-dopaminergic manifestations of PD.

P862

Deep brain subthalamic stimulation in Parkinson's disease: Effect of age

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Objective: To assess subthalamic nucleus deep brain stimulation long term outcomes in a young (Age <65 years old) and an older (Age >65 years old) parkinsonian's population.

Background: Subthalamic nucleus deep brain stimulation improves motor fluctuations and levodopa-induced dyskinesia. There is few data available about the effect of age at the moment of surgery on long term efficacy.

Design: We studied 53 consecutive patients (group I age = 58.4 ± 4.9; n = 32), (group II age = 69.6 ± 2.8; n = 21) who received implants from November 1997 through July 2003. All patients fulfilling the requirement for the United Kingdom Parkinson's Disease Society Brain Bank. They all suffered from severe motor fluctuations and dyskinesias unresponsive to medical treatment. The stereotactic procedure was based on direct MRI images targeting of subthalamic nucleus. Clinical assessment was performed preoperatively in the off-state after 12 hr withdrawal of antiparkinsonian medication. Response to L-DOPA was evaluated after taking the 1.5-fold of the usual morning levodopa equivalent dose. Tests that were performed included UPDRS part I–IV, tapping test, stand walk and sit, classification by Hoehn&Yahr stage, Schwab and England scale and cognitive functions. At the 3-month follow-up, we systematically explored the effects of the four contacts on each side to select the most effective one. Three months and 1 year after surgery, the efficacy was assessed during an acute levodopa challenge using UPDRS III in four conditions: medication ON and OFF, and stimulation ON and OFF. The same tests than preoperatively were also performed.

Results: There were not statistical differences in the two groups for sex ratio, duration of the disease, response to L-DOPA and cognitive functions (MMS, Mattis scale). For the group I stimulation reduced significantly the motor score of 62% at 3 months and 50% 1 year after surgery. For group II a decrease of 58% at 3 months and 34% at 1 year of the motor score was observed. A great reduction of levodopa-induced dyskinesia in both populations (group I: $P < 0.0001$ at 3 months, $P = 0.0028$ at 12 months; group II: $P = 0.004$ at 3 months, $P = 0.03$ at 12 months) was also observed. Intergroup comparison shown a reduction of the response to L-DOPA in group II at 12 months ($P = 0.04$). We didn't found any differences concerning tapping tests. One year after surgery the evolution of on medication Hoehn and Yahr stage evolution was worse in group II (+0.92) than in the first group (−0.42) ($P = 0.01$).

Conclusion: Despite an immediate great functional result in all patients, the time-course evolution especially for axial functions, response to L-DOPA and to stimulation are worse in the older patient group. However, a significant improvement of levodopa-induced dyskinesia was observed at 1 year in the two groups.

P863

High incidence of osteo-articular complications after STN DBS in Parkinson's disease

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Objective: To evaluate the incidence and clinical characteristics of osteo-articular complications in subjects who underwent subthalamic deep brain stimulation (STN-DBS) for Parkinson's disease (PD).

Background: STN-DBS is a recognized treatment for advanced PD patients, leading to a major improvement of motor fluctuations and significant reduction in antiparkinsonian medication. Once they have regained better motor function through STN-DBS, patients may be at higher risk to experience osteo-articular complications.

Methods: We retrospectively studied 65 consecutive patients who underwent STN-DBS for PD, identifying those who developed clinically significant osteo-articular complication following surgical procedure.

Results: Fourteen patients (21%), 6 men and 8 women, experienced osteo-articular complications 8.86 ± 13.34 months postoperatively, with an incidence of 13.8% of the patients during the first year. Traumatic complications were 1 hip fracture, 1 severe osteoporosis with rib fractures, and 1 pubo-sacral fracture, and non traumatic were 3 severe lumbo-sacral pain, 3 compressive radiculopathy, 2 lumbar canal stenosis, 2 severe shoulder arthritis, 1 knee osteoarthritis leading to prosthesis, 1 hip arthritis, and 1 decompensation of a spinal scoliosis. In nine patients, the osteo-articular condition generated significant motor impairment, mostly walking difficulties, that lasted for months. Comparison with the group of patients without osteo-articular complication showed no difference in age at the time of STN electrodes implantation (64.78 vs. 64.49, $P = 0.45$), and in pre-operative (46.86 vs. 44.76, $P = 0.30$) and 3 months post-operative (29.86 vs. 24.56, $P = 0.06$) motor UPDRS scores.

Conclusion: This study suggests that osteo-articular complications frequently occur following STN-DBS, without any significant correlation with age, sex and UPDRS scores. Improvement of motor function and increased activity in daily living after STN-DBS may be incriminated as a risk factor for such complications.

P864

Differential effects of different frequencies of stimulation of the subthalamic nucleus in treated Parkinson's disease

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Objective: To determine the effects of stimulation of STN at different frequencies in treated Parkinson's disease (PD).

Background: It has been suggested that excessive synchronisation of basal ganglia activity at low frequencies, particularly those in the tremor and beta bands, may contribute to parkinsonism [reviewed in Brown Mov Disord 2003;18:357–363]. This implies that the response to artificially synchronising activity in the region of STN may differ according to frequency. Here we synchronise STN activity by electrical stimulation of chronically implanted macroelectrodes in PD patients on antiparkinsonian drug therapy. We chose treated patients so as to limit spontaneous synchronisation (and thereby possible ceiling effects) due to the absence of dopamine.

Methods: 11 PD patients (mean age 61.1 + 2.2, 3 female) with chronically implanted STN stimulators (21 sides) were assessed after administration of their standard antiparkinsonian treatment. Several frequencies of stimulation were tested in randomised order: 0, 5, 10, 15, 20, 25, 30, 40, 70 Hz and the clinically effective frequency within that subject (*ca* 130 Hz). Bradykinesia was assessed with the BRAIN TEST which consists of rapid finger movement between two keys on a keyboard completed over 30 sec and repeated for each arm. The mean kinesia times (KT) in msec for each side (left, right) and frequency were calculated.

Results: The figure gives mean KT ± SEM. A Friedman test confirmed frequency as a main effect ($P < 0.0001$). Post-hoc two tailed Wilcoxon tests showed the following differences between KTs (all $P < 0.05$): 10 Hz KT > 20 Hz KT and 70 Hz KT, 30 Hz KT > 20 Hz or 70 Hz KT, 0 Hz KT > 70 Hz KT and, paradoxically, *ca* 130 Hz KT > 70 Hz KT.

Conclusion: The effects of stimulation in the treated state were small and (with the exception of 70 Hz) only significant relative to other stimulation frequencies rather than 0 Hz in this small sample. Nevertheless, our data support the hypothesis that there are particular frequencies of synchronisation of activity in and around STN that antagonise (10 Hz and 25 Hz) and promote (20 Hz and 70 Hz) movement. These frequencies correspond to the alpha, upper beta, lower beta and gamma peaks in STN local field potential power reported in PD [see Brown, Mov Disord 2003;18:357–363].

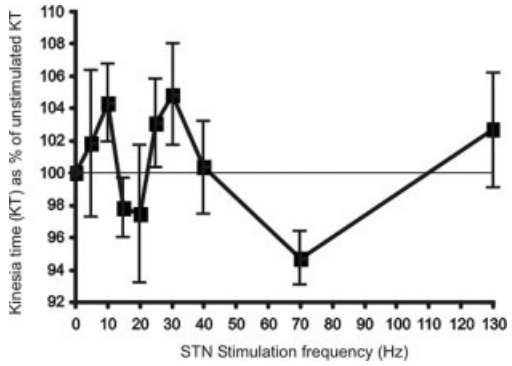

FIG. 1 (P864).

P865

Post-operative progress of severe tardive dystonia and dyskinesia following globus pallidus internus deep brain stimulation

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Objective: To evaluate the effect of chronic deep brain stimulation (DBS) of the globus pallidus internus (GPi) in tardive dystonia (TD).

Background: The medical treatment of tardive dystonia is notoriously difficult and often unsuccessful highlighting the need for new therapeutic strategies. Encouraging results after pallidotomy or pallidal DBS in levodopa-induced dystonia in Parkinson's Disease have led to renewed interest in the surgical treatment for clinically and etiologically varying forms of dystonia. To date there are only a few case reports of stereotactic procedures in medically refractory tardive dystonia lesioning different targets.

Methods: Four patients presenting with tardive dyskinesia which rapidly progressed to severe longstanding tardive dystonia were assessed before and 1, 12, and 24 weeks after bilateral GPi-DBS using the Abnormal Involuntary Movement Scale (AIMS) and the Burke, Fahn, and Marsden dystonia rating scale (BFMDRS).

Results: After 12 to 48 hr of chronic stimulation all patients experienced a major improvement in motor symptoms comprising the axial dystonic movements as well as the oro-buccal-lingual dyskinesias. During the first week the mean score of the BFMDRS part I (motor) decreased by 85% compared to baseline conditions, part II (disability) decreased by 93%, and the mean score of the AIMS decreased by 79%. No significant change of this improvement was noticed on follow-up visits at 3 and 6 month. After switching off the stimulation a nearly complete recurrence of symptoms was experienced within several minutes to 1 hr. There was no permanent morbidity or recurrence of psychiatric symptoms due to the operation or stimulation.

Conclusion: Our report suggests pallidal DBS as a highly effective treatment option in refractory tardive dystonia whereby the short delay and the extent of response alludes to a different prognosis and pathophysiology of this type of secondary dystonia.

P866

Non-microelectrode guided deep brain stimulation of the subthalamic nucleus: Safety and long-term efficacy

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The precise positioning of the stimulation electrode in deep brain stimulation of the subthalamic nucleus (STN-DBS) is crucial for the clinical outcome. The best surgical method for safe and precise implantation of the DBS electrode, however, is still controversial. Some centers regard microelectrode recordings as essential in the delineation of the STN. Other centers, however, perform the implantation without microelectrode recordings claiming a reduced risk of intracranial bleeding and a reduced time for the surgical procedure. Here we present the clinical results of 69 consecutive PD patients (33 female, 36 male) over a follow-up period of up to 3 years in whom the STN-DBS implantation was based on MRI- and CT-imaging with individual MRI-visualization of the STN and additional physiological targeting by intraoperative macrostimulation. Mean age at surgery was 60 $\pm$ 10 with a mean disease duration of 15 $\pm$ 5. Stimulation reduced OFF-motor symptoms on the UPDRS by 61% which was comparable to the L-DOPA effect before surgery. ON-symptoms were not significantly altered. While the reduction of OFF-motor symptoms remained stable over the observation period of up to 3 years an overall small increase of symptom severity most probably reflected the progression of the underlying disease. All cardinal motor symptoms were improved although for orofacial symptoms the degree of improvement was smaller than the pre-operative L-DOPA effect and even in the combination of stimulation and L-DOPA did not reach the best-ON state before surgery. Furthermore, dyskinesias were significantly reduced by some 75% on the dyskinesia rating scale. The L-DOPA equivalent dose could be reduced to 44% of the pre-surgical dosage. In this series no intracranial bleedings were observed. The main surgery- or device related complications included an infection of lead or pulse generator in 4 patients, one electrode dislocation and 2 electrode fractures, none of which resulted in permanent morbidity. Among the therapy-related side-effects dysarthrophonia and abulia were the most common observations apart from an average weight gain of 7.3 kg in the first year after the operation. These data show that good and stable clinical results of STN stimulation can be obtained without the use of microelectrode recordings and that the risk for intracranial bleeding as the most serious surgical complication appears to be small.

P867

The acute cardiovascular and respiratory effects of subthalamic nucleus (STN) and posterior hypothalamic gray matter deep brain stimulation (DBS)

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Objective: To evaluate the acute cardiovascular and respiratory effects of STN and posterior hypothalamic gray matter DBS.

Background: Kaufmann et al. showed [Neurology 2002;59:1657–1658] that heart rate (HR) increases immediately after switching on the STN DBS in 3 patients with PD, suggesting that this response may be specific to that brain region. Moreover, because the basal ganglia are considered part of the central command, they hypothesized the use of STN DBS to improve some autonomic deficits in PD.

Methods: We studied 9 patients (6 males, age = 58.7 $\pm$ 9 years) with PD with bilateral STN DBS and 5 subjects (4 males, age = 36.2 $\pm$ 9.9) with monolateral DBS of the posterior hypothalamus for controlling intractable chronic cluster headache (CH). The differences between the mean ages of the two groups were significant ($P < 0.05$). We monitored continuously HR (Grass 7P511), systolic (SBP) and diastolic (DBP) blood pressure (Portapress Model II) and respiratory rate (RE) (Grass 7P1) in two conditions: resting supine with stimulator "OFF" and with stimulator "ON". For statistical analysis (Student's t test) we considered 1 min and the 10 heartbeats before and after switching on DBS .

Results: See Tables 1–4.

Conclusion: No changes in HR, BP and RE were observed in PD and CH after switching on the stimulator either considering 1 minute or 10 heartbeats for analysis. The significant increase in SBP and DBP of PD in comparison to CH can be explained by PD's older age. Acute DBS stimulation does not influence central cardiovascular control and respiratory rate in PD and CH.

TABLE 1 (P867). *R-R intervals (mean ± SD) 1 minute and 10 heartbeats before (DBS "OFF") and after (DBS "ON") switching on the stimulator*

Patients	R-R 1 min OFF (s)	R-R 1 min ON (s)	*p*	R-R 10 beats OFF (s)	R-R 10 beats ON (s)	*p*
PD (n = 9)	0,868 ± 0,14	0,863 ± 0,15	n.s.	0,868 ± 0,15	0,870 ± 0,15	n.s.
CH (n = 5)	0,877 ± 0,06	0,846 ± 0,05	n.s.	0,883 ± 0,06	0,889 ± 0,08	n.s.
p	n.s.	n.s.	—	n.s.	n.s.	—

n.s., not significant.

TABLE 2 (P867). *SBP (mean ± SD) 1 minute and 10 heartbeats before (DBS "OFF") and after (DBS "ON") switching on the stimulator*

Patients	SBP 1 min OFF (mm Hg)	SBP 1 min ON (mm Hg)	*p*	SBP 10 beats OFF (mm Hg)	SBP 10 beats ON (mm Hg)	*p*
PD (n = 9)	135 ± 14	135 ± 117	n.s.	135 ± 14	135 ± 14	n.s.
CH (n = 5)	119 ± 11	118 ± 11	n.s.	119 ± 12	120 ± 11	n.s.
p	<0,05	<0,05	—	<0,05	<0,05	—

n.s., not significant.

TABLE 3 (P867). *DBP (mean ± SD) 1 minute and 10 heartbeats before (DBS "OFF") and after (DBS "ON") switching on the stimulator*

Patients	DBP 1 min OFF (mm Hg)	DBP 1 min ON (mm Hg)	*p*	DBP 10 beats OFF (mm Hg)	DBP 10 beats ON (mm Hg)	*p*
PD (n = 9)	74 ± 8	73 ± 9	n.s.	73 ± 8	73 ± 8	n.s.
CH (n = 5)	65 ± 9	65 ± 9	n.s.	65 ± 10	65 ± 9	n.s.
p	<0,05	<0,05	—	<0,05	<0,05	—

n.s., not significant.

TABLE 4 (P867). *RE 1 minute before (DBS "OFF") and after (DBS "ON") switching on the stimulator*

Patients	RE 1 min OFF	RE 1 min ON	*p*
PD (n = 9)	24	24	n.s.
CH (n = 5)	18	17	n.s.
p	<0,005	<0,005	—

n.s., not significant.

P868

Effect of STN stimulation on perceptual and acoustical assessements of dysarthria in patients with Parkinson's disease: Preliminary results

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Objective: To ascertain the impact of subthalamic nucleus deep brain stimulation (STN-DBS) on speech in patients with Parkinson's disease (PD) using perceptual and acoustical measures.

Background: STN-DBS is known to be efficient for the improvement of limb movements, and some motor aspects of speech production [Pinto et al., 2003]. However, dysarthria is a symptom less predictable than global motor disability in terms of response to STN-DBS, and it seems that hypophonia and lack of intelligibility tend to persist after surgery. It is still unclear what components of speech may improve, remain or even worsen with STN-DBS, which could be useful in order to inform clinical practice.

Methods: Three patients with PD (age range 46–54 years, duration of disease range 13–20 years) have been assessed with normal medication, before and after STN-DBS. Perceptual analysis of speech has been carried out using the Assessment of Intelligibility of the Dysarthric Speech scale [AIDS, Yorkston et al., 1981]. Acoustical recording (Microphone ECM, MS957, Sony; DAT recorder, model PDR 1000TC, HHb) of sustained vowel /a/ provided analysis (Computerized Speech Laboratory, CSL 4300b, Kay Elemetrics) of sound pressure level (SPL), maximum sustained phonation (MSP) and fundamental frequency (F_0).

Results: Despite a deterioration of intelligibility (AIDS score = 85% pre-surgery, 60% after), STN-DBS improved significantly most of acoustical parameters for patient 1: SPL (50 dB pre-surgery, 65 dB after) and MSP (4 sec pre-surgery, 15 sec after) increased, and F_0 remained stable (90 Hz pre-surgery, 88 Hz after). For patient 2, a post-surgical impairment of intelligibility (AIDS score = 87% pre-surgery, 75% after) was also observed, whereas no effect on acoustical parameters was noted. Patient 3, who did not suffer from severe dysarthria, did not present any change in both acoustical and perceptual assessments before and after STN-DBS.

Conclusion: These preliminary results are part of a prospective study that will include consecutively all patients with PD operated in our neurosurgical centre. They suggest that no correlation should be made between perceptual and acoustical evaluations: motor subcomponents of speech production may be improved by STN-DBS although a worsening of intelligibility can be observed. It must be emphasised that motor coordination in PD dysarthria, assessed perceptually, seems to be less responsive to STN-DBS than speech organ movements, described by most of the electrophysiological studies up to now.

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Deep brain stimulation of the STN activates the electrode target area in patients with advanced Parkinson's disease

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Objective: The effect of STN stimulation on its neuronal target structures, e.g., inhibitory or excitatory, as well as the target tissue, e.g., cell bodies or fibre tracts or both, are currently under debate. To address these questions, we measured the resting cerebral metabolic rate of glucose (rCMRGlc) with [^{18}F]fluorodeoxyglucose (FDG) and positron emission tomography (PET) in 11 patients with advanced PD (7 males, 4 females, age [mean ± SD] 61.8 ± 7.7 years, disease duration 14.9 ± 4.7 years) 4 months after implantation in the STN-DBS off- and on-condition and in 10 healthy age-matched controls (6 males, 4 females, age 62.6 ± 3.6 years).

Methods: Final x-y-z coordinates of active electrode poles were determined with intra-operative skull x-ray and subsequently transferred to individual MRI scans. Subsequently, a spherical volume-of-interest (electrode-VOI, 5 mm diameter) was defined with the active electrode pole as center on MRI scans (3D-Tool). Other VOIs were STN, Head of the Caudate, Pallidum, and Putamen. Quantified FDG-PET scans were exactly matched to these MRI atlases and the rCMRGlc normalized for global brain activity was calculated within each VOI.

Results: In the DBS-on condition, the rCMRGlc significantly increased in the electrode-VOI compared with the off-DBS state (absolute 19.4 ± 3.0 vs. 16.0 ± 2.7 μmol/100g/min and normalized 0.79 ± 0.10 vs. 0.71 ± 0.09, $P = 0.001$, paired t test). Moreover, a non-significant activation occurred within the STN under stimulation (absolute 19.7 ± 3.0 vs. 16.8 ± 3.3 μmol/100 g/min and normalized 0.81 ± 0.11 vs. 0.75 ± 0.11, $P = 0.088$, paired t test). Compared with controls, PD patients had significantly higher normalized rCMRglc within the putamen in both DBS-conditions ($P < 0.01$, unpaired t test).

Conclusion: Metabolic activation in the DBS target region seems to occur which suggests rather activating than inhibitory stimulation effects on neuronal cell bodies or axons leading to an increased output from the stimulation site onto afferent structures via ortho- or antidromic fibre conduction. Therefore, our study results indicate a stimulation effect fundamentally different from lesional procedures in the STN target. We propose that our PET findings most likely reflect neuronal jamming of the STN and its projection sites. Pathophysiologically, long-standing high-

frequency activation of the STN target region might replace an abnormal phasic firing pattern in the pallidal outflow pathway, which was identified as a key feature of the parkinsonian state, with a high-frequent, tonic activity state that does not longer imply abnormal sense for the generation of parkinsonism.

P870

Is bilateral stimulation of the subthalamic nucleus less effective in Parkinson's disease when procedure is done under general anesthesia? A prospective study of 75 patients

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Objective: to assess the long-term effect of bilateral chronic subthalamic nucleus (STN) stimulation after a general anesthesia (GA) procedure.

Background: A precise localization of the electrode is required to obtain the best clinical improvement with STN stimulation. Optimized choice of the final electrodes localization is based on a rigorous protocol defined by Limousin et al. [1995]: anatomical targeting, electrophysiological recording and clinical testing with stimulation. This evaluation needs that the patients remained awakened and cooperative despite important stress and fatigue during the operation. Alternative procedures, which may be more comfortable have not been evaluated.

Methods: We evaluated 75 consecutive patients (56 men, mean age:60 ± 8.3 years, mean Hoehn&Yahr score: 3.8 ± 0.8) treated by bilateral chronic STN stimulation. Assessments were performed before and every 6 months from 1 to 3 years after surgery. Strereotactic MRI and electrodes implantation were performed under a single light GA (sevoflurane + alfentanyl) that allowed us to record a typical STN signal in all patients (5 microelectrodes on each side). Under this procedure detection of capsular side effects induced by stimulation was possible. Evaluation of IPDRS, Beck Depression Inventory, Mattis Dementia Rating Scale (MDRS), PDQ39 and psychiatric follow-up was done pre and postoperatively.

Results: Five serious postoperative adverse events occurred: one transient delirium, one general infection requiring temporary removal, one pulmonary embolism and one electrode repositioning. The motor disability was improved by 67% (mean motor score while off medication before surgery (43 ± 13) compared to the last evaluation performed after surgery (mean: 24 months) while Off-medication/On-stimulation (14 ± 8)). Activity of daily living (UPDRS II) improved by 47% in Off condition. The dose of dopaminergic treatment was reduced by 60.2%. MDRS score remained unchanged in 72 patients. The main behavioral change observed in almost 30% of the patients was a reduction of spontaneous activity (apathy) despite the dramatic motor improvement. New cases of depression were not found, no suicidal risk was noted, 2 transient hypomania resolved without specific therapy.

Conclusion: Comparison of these results to the main previous studies, which used local anesthesia shows no significant difference. The peroperative microelectrode recording and the detection of the most severe side effects induced by capsular stimulation are still reliable but are conditioned to a specific GA procedure. Immediate postoperative follow-up was simple. The efficacy of STN stimulation is not modified by GA, which gives more comfort to the patient. Nevertheless, the procedure still requires a very rigorous technique at each step: carefully selected patients, high quality anatomical targeting, multiple microelectrodes recording.

P871

Long-term outcomes of bilateral stimulation of the subthalamic nucleus in patients with advanced Parkinson's disease

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Objective: To evaluate long-term outcomes of patients with advanced Parkinson's disease (PD) treated with bilateral deep brain stimulation (DBS) of the subthalamic nucleus (STN).

Background: In patients with advanced PD, STN DBS has been shown to improve motor function and decrease antiparkinsonian medication requirements. However, there is still sparse data on the long-term effects of the procedure. We report outcomes from a cohort of 38 patients who had bilateral STN DBS between 1999 and 2001 who were followed prospectively up to four years after surgery.

Methods: We evaluated patients preoperatively, 12 months after surgery, and at a long-term follow-up visit using the Unified Parkinson's Disease Rating Scale (UPDRS) and the Dyskinesia Rating Scale. Ratings were performed both on and off dopaminergic medications. We compared postoperative UPDRS total scores, UPDRS subscores, dyskinesia ratings, and medication dosages with preoperative baseline values.

Results: Thirty-one patients had follow-up 12 months after surgery; 30 patients had long-term evaluations beyond one year (median duration 30.2 months, range 13.4–44.7 months). Total UPDRS scores in the off-medication state were improved by 37% ($P < 0.001$) at 12 months and 20% ($P = 0.002$) at the long-term evaluation. Off-medication UPDRS part III scores were significantly improved at both one year and at the last evaluation (41% and 34%, $P < 0.001$). Motor subscores for bradykinesia, rigidity, and postural instability showed continued improvement over baseline, although the gains in postural stability diminished after the first year. Tremor scores were markedly improved at one year (75%, $P < 0.001$), but were not significantly improved over baseline at the later assessment. Dopaminergic medication requirements were decreased by 42% ($P < 0.001$) during the first postoperative year and remained below preoperative levels at long-term follow-up (24% reduction, $P = 0.002$). Average duration of "off" time remained decreased by about 40% at both one year and the time of last evaluation ($P < 0.001$). Patients had a sustained marked reduction in dyskinesia severity (75% at 1 year and 67% at long-term evaluation, $P < 0.001$).

Conclusion: In this cohort of patients with advanced PD, bilateral STN stimulation improved motor function and reduced medication requirements for up to four years after surgery. We conclude that STN DBS is an effective long-term therapy for selected patients with advanced PD.

P872

Effects of STN DBS in post pallidotomy patients: Clinical and neurophysiologic results

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Objective: S: 1- To evaluate the effects of bilateral Subthalamic DBS in Parkinson's disease (PD) patients who have previously undergone unilateral pallidotomy; and 2- To examine the impact of the pallidotomy on the electrophysiological properties of the patient's subthalamic nuclei (STN).

Methods: Clinical series of 19 patients who underwent implantation of bilateral STN stimulators an average of 5.8 ± 1.7 years (Range: 3 to 8) following unilateral pallidotomy. The cohort represents the combined experience of two surgeons (JE, RA) who work with the same neurophysiologist (JS). Clinical and electrophysiologic data were collected via retrospective chart review. The motor sub-score of the Unified Parkinson Disease Rating Scale (UPDRS III), 12 hr off medications served as the primary clinical measure. In order to compare the effects of STN DBS ipsi- and contralateral to the previous pallidotomy, categories that measure axial symptoms were eliminated.

Results: Three months after surgery the mean off medication UPDRS-III score was improved 49.5% (44.7 pre-op vs. 20.9 post-op; $P < 0.001$, Paired Student's T-test). The improvement was asymmetric. The UPDRS III scores for the previously untreated side improved 48.8% (Pre: 16.6 ± 2.8, Post: 8.5 ± 3.7, $P = 0.002$) as compared to a 27.0% (Pre: 13.7 ± 4.8, Post = 10 ± 3.5, $P = 0.1$) improvement on the side previously treated with pallidotomy. Electrophysiologically, the mean firing rates of STN neurons were statistically the same on both sides (42.7 ± 43.2 vs. 36.9 ± 37) ; however, the variance in the firing frequency was significantly lower ipsilateral to the previous pallidotomy (67.6 ± 66.9 vs. 122.2 ± 121.4).

Conclusion: Bilateral subthalamic DBS is a safe and effective intervention in patients with idiopathic PD who have previously undergone unilateral pallidotomy, although the improvement in motor function is more robust on the previously untreated side. Pallidotomy alters the variance in the mean firing rate of ipsilateral STN neurons.

P873

Noninvasive experimental and clinical DBS lead/extension failure testing

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Objective: Noninvasively localize faults in the implanted DBS system.

Background: Employing standard EMG electrodes, one can observe the electrical impulses conducted along an implanted stimulating system and thereby evaluate the integrity of the conduction pathway. We have adapted this concept to localize faults within the lead or extension of malfunctioning neural stimulating systems noninvasively.

Methods: Standard EMG electrodes are placed two inches apart, overlying a given segment of the implanted system. The ground is placed over the pulse generator. The EMG machine (Nicolet Viking II) is set in 'free running' mode (frequency range: 0.5 Hz–3,000 Hz). By comparing the recorded wave morphologies across each monopolar and bipolar stimulator setting and to a set of test bed recordings, one can determine the type and location of many faults.

Results: Ten malfunctioning neural stimulation systems were evaluated using this technique (eight sub-cortical systems and two spinal cord systems). Failures were properly localized in six of the ten devices, as confirmed following removal of the affected components. In two instances we failed to exhibit a conduction defect although one existed. In one instance the pulse generator was completely depleted due to a short in the extension cable, making it impossible to apply this technique. In one instance, the site of the fault was incorrectly localized due to the proximity of the active and reference electrodes during the test.

Conclusion: When standard device interrogation techniques and X-rays cannot determine or localize problems within a neural stimulation system, surface EMG techniques can be used to localize the fault.

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DBS electrode contact and stimulation frequency effect on parkinsonian symptoms

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Objective: To prospectively evaluate the therapeutic efficacy of subthalamic deep brain stimulator settings of contact, frequency, and overall energy for treating the symptoms of Parkinson's disease.

Background: Observations at our institution have demonstrated that specific PD symptoms are more responsive to stimulation at specific anatomic locations as determined by DBS contact position. Using neural response properties to electrical stimulation and the anatomic location of key fiber tracts these results can be explained.

Methods: Patients were selected once stable and effective stimulation settings were found, and all patients were randomized to receive either constant voltage (2.5–3.0 V) or constant energy (varying voltage to compensate for energy changes from the predetermined frequency settings) throughout the study. Patients were set bilaterally to a range of five stimulation rate settings (5 Hz, 60 Hz, 100 Hz, 135 Hz, 185 Hz) at each contact (0−,C+; 1−,C+; 2−,C+; 3−,C+) and were evaluated for tremor (UPDRSIII, Tremor Rating Scale), rigidity (UPDRSIII), bradykinesia (UPDRSII I), dyskinesia (dyskinesia rating scale, abnormal involuntary movements scale), and overall symptomology (UPDRSIII). All patients were evaluated identically while both off and on medication. Evaluation scores were analyzed for relative effectiveness of parameters for treating specific symptoms.

Results: Our preliminary data (n = 3) show that the lower contacts (0−,C+ and 1−,C+) are most effective in treating rigidity and tremor. In addition, rigidity improvement scores trend directly with increasing energy levels. Adverse effects of difficulty swallowing and speaking, stimulation-driven tremor (5 Hz), lightheadedness, profuse sweating, and visual field disruption were more easily obtained at more ventral contacts, requiring 50% or less energy at contacts 0 and 1 than at contacts 2 and 3. While dyskinesias were easily induced at contact 0 (severity increasing directly with energy), we cannot yet assess the full affects of DBS setting for treating dyskinesia as none of the three patients suffered from significant levodopa-induced dyskinesias.

Conclusion: Current results provide some insight into the affects of STN-DBS. Due to the small number of patients no statistical relevance can yet be determined.

P875

Frameless placment of deep brain stimulation electrodes: An accuracy study

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Objective: To evaluate the accuracy of a frameless method for deep brain stimulator placement as compared to traditional frame-based methods.

Background: Deep brain stimulation (DBS) has become a well-established treatment for Parkinson's disease and other movement disorders. DBS electrodes are traditionally placed using a stereotactic frame, which can be uncomfortable for the patient and which requires the coupling of imaging and surgery. Frameless techniques offer advantages of patient comfort, decoupling of imaging from surgery, and the opportunity to incorporate real-time tracking of electrode position.

Methods: A three-phase multi-center study was designed to evaluate the accuracy of a frameless system for the delivery of DBS electrodes. In phase one, 135 localizations of a standardized target within a stereotactic phantom were carried out at 6 centers using the frameless device. In phase two, a stereotactic frame was used to confirm the trajectory in 21 DBS electrode placements. Final electrode position was measured on postoperative CT scans and compared to the planned position. In the third and final phase, the frameless device was used alone in 16 implants and the postoperative electrode position again compared to the planned preoperative position.

Results: In phase one, the mean localization error of the frameless system was 0.98 mm with a 99% confidence interval of 0.86 to 1.10 mm. In phase two, mean localization error was x - 1.62 mm, y - 1.09 mm, and z - 2.26 mm. In phase three, mean localization error was x - 1.32 mm, y - 1.49 mm, and z - 1.64 mm.

Conclusion: Accuracy of frameless deep brain stimulator placement compares favorably with that achievable using a stereotactic frame, matching published accuracy data.

P876

Effects of GPi stimulation on perceptual and acoustical features of dysarthria in patients with generalized dystonia: Preliminary results

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Objective: To ascertain the impact of internal globus pallidus deep brain stimulation (GPi-DBS) on speech in patients with generalised dystonia using acoustical and perceptual measures.

Background: Generalised dystonia can be defined as a syndrome dominated by sustained muscle contractions, frequently causing twisting and repetitive movements, or abnormal postures. It can affect different parts of the body, such as mandibular and facial regions, neck and laryngeal muscles. As a result speech can be affected in different degrees, leading to substantial loss of communication. GPi-DBS has proven to be effective for most dystonic syndromes, particularly in the disease due to DYT1 mutation [Coubes et al., 2000]. However, no studies have been carried out so far to evaluate specifically the effects of GPi-DBS on speech in patients with dystonia.

Methods: Three patients (age range 26–30 years) with generalized dystonia have been assessed before and after GPi-DBS. We used the Burke-Fahn-Marsden dystonia movement and disability scales (BFM-DMDS) in order to evaluate their global motor state. Perceptual analysis of speech has been carried out using the Assessment of Intelligibility of the Dysarthric Speech scale [AIDS, Yorkston et al., 1981]. Acoustical recording (Microphone ECM, MS957, Sony; DAT recorder, model PDR 1000TC, HHb) of sustained vowel /a/ provided analysis (CSL 4300b, Kay

Elemetrics) of sound pressure level (SPL), maximum sustained phonation (MSP) and fundamental frequency (F0). Among these 3 patients, the last 2 had no functional speech before surgery.

Results: For patient 1 (FBM-DMDS 82/150 pre-surgery, 49/150 post), AIDS score improved from 12% pre-surgery to 95% post, as well as MSP (3 sec pre, 8 sec post) and SPL (25 dB pre, 45 dB post). Patients 2 and 3 (FBM-DMDS scores 142/150 pre-surgery, 128/150 post; and 116/150 pre-surgery, 106/150 post), with the most severe dysarthria pre-surgery, showed improvement in control of vocalisation but that did not reach significance in acoustical analysis. However, this improvement allowed them to have a reliable Yes/No response. Improvement of upper limb movement led to the use of communication and environmental aids, which was not possible before surgery.

Conclusion: These preliminary results are part of a prospective study that will include consecutively all patients with generalized dystonia operated in our neurosurgical centre. They suggest that speech can be improved by GPi-DBS in patients with dystonia, and the variable efficacy of the treatment reflects the partial role of subcortical structures in speech motor control. However, where perceptual assessment fails to capture improvement induced by GPI-DBS in this variable population, electrophysiological tools would be more appropriate to analyse changes of oral motor control.

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P877

The role of the subthalamic nucleus in language processing: Microelectrode recordings prior to the implantation of deep brain stimulation electrodes for people with Parkinson's disease

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Objective: To evaluate the role of the subthalamic nucleus (STN) in language processing in patients with Parkinson's disease (PD). Microelectrode recordings obtained prior to the insertion of deep brain stimulation (DBS) electrodes, will be analysed to investigate the STN's role in language processing. More specifically, the aim of the present study is to investigate the difference between the dominant and nondominant STN in semantic processing and the role of the STN in the processing of words with negative emotional valence.

Background: Recent studies have implicated the STN in language processing, as measured through functional changes in verbal fluency, discourse, lexical decision and high-level language, after patients with PD have received DBS of the STN. The surgical procedure of DBS with the use of microelectrode recordings for identification of the STN in surgery, allows for the unique opportunity to investigate the neuronal activity of the dorsolateral STN while patients are performing language tasks, and therefore further define the role of the STN in language processing.

Methods: Two language tasks were performed intraoperatively by a series of patients with PD, prior to the implantation of DBS electrodes. The first task involved the auditory presentation of two words, either belonging to the semantic category of animals or household items. The participants were required to manually respond as to whether the two words belonged to the same semantic category (e.g., *cat–dog* or *door–chair*) or different semantic categories (e.g., *cat–chair*). The second language task required the participants to listen to a series of words that carried negative emotional valence (e.g., *poverty* or *cancer*) or were neutral in emotional valence (e.g., *clock* or *hat*). Participants were again required to respond by manually depressing a response button to indicate negative or neutral. Microelectrode recordings were obtained from both the left and right STN during the completion of these tasks.

Results: Preliminary findings from a series of patients will be presented and discussed in relation to changes in neuronal activity as a function of left or right STN and task condition. In addition, behavioural data, such as reaction time and error rate analyses will also be presented.

Conclusion: The use of microelectrode recordings prior to the implantation of electrodes for DBS provides not only a useful technique in the surgical guidance of subcortical regions, but also allows the opportunity to investigate the role of these structures in language processing.

P878

Oculomotor sub-region within the STN: Evidences from DBS in PD

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Objective: To compare the coordinates of the point producing gaze deviation during peroperative macrostimulation and the coordinates of the electrode leading to best postoperative motor response in Parkinson's disease (PD) patients treated by STN DBS

Background: According to current models of basal ganglia the subthalamic nucleus (STN) is connected with the cortex and thalamus through loops subserving motor, prefrontal, limbic and oculomotor functions. Primate studies have shown that motor and oculomotor areas are segregated within the STN, but this has never been proved in humans. STN DBS is currently used to treat advanced PD patients with motor fluctuations. During STN DBS implantation gaze deviation may be observed during macrostimulation used to determine best motor response.

Methods: During the macrostimulation period of the MRI-micro-macrostimulation guided stereotactic implantation of STN DBS in a cohort of 50 consecutive PD patients, we observed contraversive slow tonic gaze deviation at one side in 8 patients, and at both sides in 7 patients. Intraoperative macrostimulation at 2, 50, 200 Hz were performed from 6 mm above to 2 mm under target. The 3D localization of the electrodes was controlled postoperatively on 3D MRI according to the AC-PC referential (midcommissural point as origin) using trigonometric and Pythagorean relations. This position was assumed to be similar to the macrostimulation electrode, as final electrodes were implanted after one trajectory. The 3D position of the mean oculomotor points that lead to gaze deviation and the position of the contact producing greatest reduction in UPDRS motor scale were compared using paired and unpaired Students t-test analysis. Values of $P < 0.05$ were considered statistically significant

Results: The mean coordinates of the oculomotor points that lead to gaze deviation were: AP −2.28 mm, LAT 11.95 mm, VERT −2.45 mm. These coordinates were significantly different from those of the contact producing greatest reduction in UPDRS motor scale: AP −3.28, LAT 11.12, VERT −4.29. The point inducing gaze deviation was projected in the ventral part of the STN and the best motor point in its dorso-lateral part.

Conclusion: We found that eye movements could be elicited within a specific area of the STN that was significantly different from the area producing best reduction in UPDRS motor score. Based on the fact that STN stimulation increases activity of specific parts of the prefrontal cortex, we hypothesize that slow tonic gaze deviation could result from activation of the frontal eye field system. Our finding is the first confirmation of a specific region for eye movements within the STN similar to other primates.

P879

Modulation of executive functions by frequency settings in subthalamic deep brain stimulation

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Objective: We compared verbal fluency (VF) in patients with Parkinson's disease (PD) during high frequency (HF) and low-frequency (LF) deep brain stimulation (DBS) of the subthalamic nucleus (STN) to examine whether LF-STN-DBS in contrast to HF-STN-DBS has a positive effect on executive functions.

Background: High-frequency STN-DBS improves motor functions of PD but may worsen executive functions like verbal fluency by affecting pathways to the prefrontal cortex. In contrast, LF-STN-DBS leads to deterioration of motor functions possibly by enhancing pathological synchronization. It is not known whether LF-STN-DBS has also an effect on

executive functions and could improve for example verbal fluency by activating pathways to prefrontal areas.

Methods: We examined four different verbal fluency subtests under double-blind conditions in 12 PD-patients 3 or more months after bilateral elektrode-implantation into the STN. After overnight withdrawal of dopaminergic medication we randomly changed stimulation frequency between no stimulation, 10 Hz (LF) and ≥130 Hz (HF). Stimulation was kept constant with respect to pulse width, voltage and pole of stimulation. Fifteen minutes after change of stimulation frequency VF was tested in different parallel test versions. The experimental design was randomised in order and balanced with regard to stimulation frequency and test version. Mean number of words at each frequency was compared for the sum of all subtests and for each subtest separately.

Results: VF was significantly better at 10 Hz (48.3 words) compared to 130 Hz, and showed a non-significant trend towards worsening at 130 Hz (42.3 words) compared to no stimulation (43.8 words). These results were consistent across all subtests.

Conclusion: The present study provides evidence for a beneficial effect of low-frequency (10 Hz) STN-DBS on verbal fluency. It is possible that this effect is caused by activating neural pathways projecting to the prefrontal cortex. Additionally the study reproduces the negative effect of therapeutic high-frequency STN-DBS on verbal fluency. Taken together the present study provides evidence for a frequency dependent tuning of cognitive circuits involving the STN.

P880

Deep brain stimulation for Parkinson's disease: Assessement after 13 cases

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Objective: To share the experience of Hospital S. João in Deep Brain Stimulation (DBS) of subthalamic nucleus. Results attained in initial and consecutive thirteen patients with Parkinson's disease (PD) submitted to this procedure are discussed.

Background: Prevalence of PD is about 1/1,000 and 5% of all PD patients present with symptoms before age of 50. These are in general the best candidates for surgical treatment, before development of major disability that threatens employment and role in family and society. Selection is based in several criteria: patients with less than 70 years old, advanced stage PD with at least 5 years of evolution, not optimally managed by medication are candidates. Dopaminergic stimulation (L-DOPA and agonists) with at least 30% reduction of the part III UPDRS (ideal response: above 80%) and MRI with no significant lesions are required. Dementia and severe depression are exclusion criteria. DBS of subthalamic nucleus is expected to reduce major motor manifestations and drug intake. A decrease of 60% in UPDRS (part III), 80–90% in levodopa-induced dyskinesias and about 80% in tremor is also expected, as well as disappearance or reduction of OFF-periods and OFF-dystonia.

Methods: From October 2002 to December 2003, 13 patients, ten male and three female with a mean age of 56 years (min: 32; max: 69), with 13.8 years of disease duration (mean) were submitted to DBS of subthalamic nucleus. UPDRS is evaluated before surgery in ON and OFF medication periods, and after surgery, in ON and OFF stimulation state (with no medication). Neuropsychological tests are applied before surgery as well as in the 6th and 18th months after the procedure. Subthalamic nucleus is located by means of stereotaxic CT scan and MRI fusion imagery. Five microregister electrophysiological recording and microstimulation electrodes define the target area in the per-operative period. Quadripolar electrodes (DBS3389, Medtronics®) are implanted bilaterally in a single operative time.

Results: The UPDRS part III before surgery was in OFF: 46.7 (min: 27; max: 66) and ON: 11.7 (min: 4; max: 26). UPDRS part III was evaluated in off-medication state with stimulation switched ON in several assessment after surgery with a median score of 18.69 (min: 9; max: 40.5). Reduction in OFF periods was observed in all but one patient. Dyskinesias persist in only one patient. In average L-DOPA dose was reduced 45% on 10 of the 13 patients. Adverse effects related with surgery were: intraventricular haemorrhage in one patient and local inflammatory reaction to neurostimulation unit in another one. A misplaced electrode was replaced in one patient.

Conclusion: Subthalamic nucleus DBS seems most useful for relatively young patients who have motor complications from Levodopa and are independent in activities of daily living in their best on-medication state, so selection of patients is very important. Adverse effects of the procedure are rare, but can be severe. Our initial experience in subthalamic nucleus DBS shows that this treatment is very effective in some patients with advanced forms of PD and badly ranged with medication.

P881

The additive effect of subthalamic nucleus stimulation and medication on motor scores in Parkinson's disease

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Long-term stimulation of the subthalamic nucleus (STN-DBS) improves parkinsonian symptoms, particularly motor fluctuations, lessens "off" periods, allows for reduction in medication and decreases dyskinesia. It has been widely reported that stimulation produces "on" periods no better than obtained by medication alone, but for more of the day and with less dyskinesia. However there have been conflicting results about stimulation and medication having any additive effect on UPDRS "on"scores.

We report on our results after one year of bilateral STN stimulation in 18 Parkinson's disease (PD) patients. All assessments "on medication" were performed using the same levodopa equivalence pre and post operatively in each patient. There was an improvement in the 'off' state. The postoperative mean total UPDRS part III motor scores "off medication/on stimulation" scores improved by 41% compared to preoperative "off medication", ($P < 0.001$, Wilcoxon paired t test). In addition, mean part III scores for "on medication" preoperatively, compared to postoperative "on medication/on stimulation" showed a 31% improvement ($P < 0.05$, Wilcoxon paired t test). Sub-score analysis showed 81% improvement in tremor ($P < 0.05$), and 63% in rigidity ($P < 0.01$). Changes in bradykinesia scores were not significant. Comparison of the mean total UPDRS part III motor scores postoperatively "on stimulation/off medication" and "on stimulation/on medication" were also improved by 45% ($P < 0.001$). On part IV of the UPDRS the duration of dyskinesia was reduced from a mean time of 26–50% to 0–25% of the day. The mean scores for duration and disability of dyskinesia (questions 32,33,34) pre-operatively was 5.8, range 1–10, post operatively this improved with a mean of 1.8, range 0–4 ($P < 0.001$). 'Off' period duration was also reduced, from 26–50% to 0–25% of the day. Total levodopa equivalent medication was reduced by 36.7% compared to preoperatively.

Therefore, we show that there is an improvement in "on" UPDRS scores when "on stimulation/on medication", compared to "on medication" scores preoperatively and postoperatively.

Large reductions in medication dosages postoperatively may not give the patient the best results. Surgery may permit lowering of medication and improvement in dyskinesia. However, our results show stimulation and medication produce better motor scores than medication or stimulation alone, suggesting an additive effect. Too great a reduction in medication may result in suboptimal "on" period quality. The exact mechanism by which STN-DBS and levodopa has an additive effect is unclear. STN-DBS significantly improves bradykinesia, but there is no additive effect of levodopa on this symptom in contrast to tremor and rigidity. This suggests that dopaminergic medication and STN-DBS might work via different mechanisms. Further work is required to explain this.

P882

The ultrastructural analysis of the surface of explanted deep brain stimulation electrodes with scanning and transmission electron microscopy

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Introduction: Deep brain stimulation (DBS) is used to treat a variety of severe medically intractable movement disorders. A single previous study [Haberler et al. Ann Neurol 2000;48:372–376] examined the brains of 8 PD

patients treated with DBS, concluding that chronic DBS caused only mild gliosis around the lead track and no damage to brain tissue.

Hypothesis: An explanation of the above finding is that the interface between the DBS electrode and brain tissue was attached to the DBS electrode, which when removed left undamaged brain.

Methods: 1 control and 18 (1 subthalamic nucleus and 17 globus pallidus internus) explanted DBS electrodes were prepared (after fixation in 3% glutaraldehyde) for scanning (SEM: n = 7) or transmission (TEM: n = 9) electron microscopy or both (n = 2) according to departmental protocol. The electrodes were sourced from 1 patient with PD, 1 with myoclonic dystonia (MD), 2 with cervical dystonia (CD) and 5 with generalised dystonia (GD) and had been in situ for 11 months (PD), 16 months (MD), 14 and 24 months (CD) and mean: 12 (range: 3–24) months for GD respectively.

Results: A foreign body multinucleate giant cell reaction was present in all TEM samples and in SEM samples pre-washed to remove blood and fibrin. Mononuclear macrophages containing lysosomes were also present on TEM. Both types of cell contained electron dense inclusions, which were also present adjacent to these cells.

Conclusion: DBS electrodes cause a foreign body giant cell reaction around them irrespective of duration of implantation. This may be relevant to the clinical course of response to DBS in patients with various forms of dystonia.

P883

Long-term result of treament for essential tremor with stimulation of the subthalmic nucleus: Case studies

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Objective: To test the long-term effects of STN as a target for DBS-treatment of essential tremor.

Background: ViM-stimulation can generally be effective in the treament of essential tremor. The effect, however, often diminishes over time. In an effort to test if STN could be a suitable target for treatment of essential tremor and supply a more durable tremor control a few patients were tested in our clinic. Both ViM and STN were targeted and stimulated intraoperatively. Some of these patients received STN-electrodes. We now report a six year follow-up.

Methods: Six patients were subjected to peroperative stimulation in ViM and STN. The target yielding the best result was chosen for implantation. If results were equally good at both targets the STN target was used. Thus three of these patients received unilateral STN-stimulation and three unilateral ViM stimulation.

Results: The three patients receiving STN-stimulation still have good tremor block with unchanged (in one case slightly increased) stimulation intensity. The voltage requirement has been low and for none of these patients exchange of the stimulator has become necessary. Follow-up of the three patients where ViM was the better target is more difficult to interpret: two of these patients have died, from un-related causes, during the follow-up period. The third patient has had replacement of battery and despite increase in stimulation intensity the tremor-blocking effect has diminished.

Conclusion: In this very small group treatment of essential tremor by electrical stimulation of the STN seems to give a more long-lasting effect at a lower stimulation-intensity than ViM.

P884

Mechanisms of body weight gain in parkinsonian patients after subthalamic stimulation: Implication of changes in energy expenditure

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Objective: The implication of changes in energy expenditure (EE) in the mechanisms of body weight gain after chronic subthalamic bilateral stimulation was evaluated in parkinsonian patients.

Background: Chronic bilateral subthalamic stimulation leads to a spectacular improvement in patients with motor complications, such as levodopa-induced dyskinesia and motor fluctuations. However, weight gain of approximately 8% of initial body weight has been observed 3–6 months after surgery. Twenty kilogram weight gain may even occur in some patients during the first year following the surgery.

Methods: Six parkinsonians aged 60 ± 7 years were examined one month before and three months after surgery. Examinations included body composition determination using DEXA and EE measurements 1) during 36 hr in indirect calorimetric chambers while physical activity (sleep, resting activities, meal, 3 or 4 times 20 min cycling at 13 km/hr) and food intakes were rigorously controlled, 2) in resting conditions during a levodopa (before surgery) or stimulation (after surgery) challenge in the "off" and "on" conditions. Ethical agreement was obtained and French legislation (Huriet law) was obeyed.

Results: The patients gained on average 3.0 ± 2.8 kg after the surgery ($P < 0.05$). Fat free mass was significantly increased by 1.9 ± 1.5 kg ($P < 0.05$) while fat mass was not significantly altered (1.1 ± 2.6 kg). Before surgery, EE measured in the calorimeters was similar to that of healthy subjects matched for age and body composition. By contrast, it was increased by 50–80% (depending on the subject) during episodes of "off" periods. In resting conditions, EE was increased by 14.6 ± 13.4% in the "off" condition (i.e., without levodopa) ($P < 0.05$). After the surgery, 24 hr EE measured in the calorimeters tended to be lower than before (−9.3 ± 10.9%, $P = 0.08$). EE during sleep increased by 10.6 ± 9.4% ($P < 0.05$) while EE during resting activities and during cycling was not significantly altered. By contrast, EE during meal was significantly decreased by 15.6 ± 13.5% ($P < 0.05$). In resting conditions, EE was increased by 19.1 ± 36.7% in the "off" condition (i.e., without stimulation) (P = NS).

Conclusion: Parkinsonian patients receiving levodopa have a normal energy metabolism except during the episodes of akinesia which are characterized by highly increased EE. After surgery, fast body weight gain is observed. Decrease in 24 hr EE, probably due to the absence of motor fluctuations, may be one of the cause. However, increased energy intake or decreased physical activity may be also involved.

P885

Stimulation of the thalamic ventralis intermedius nucleus (VIM) improves main components of ataxia in multiple sclerosis patients

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Background: Ataxia is a common symptom in multiple sclerosis (MS), which is hardly improved by pharmacological treatment. The clinical phenomenon ataxia includes an impaired timing and an impaired energizing of muscles resulting in a disturbed movement.

Objective: The aim of our study was to analyze the effect of contralateral VIM stimulation on these parameters during alternating movements in patients with MS.

Methods: We investigated 6 patients with a primary (n = 1) or secondary (n = 5) chronic progressive MS (range 36–66 years, median 41.5 years). The patients sat in a chair with one arm abduced rectangularely. This arm was strapped into a splint with one fixed section for the upper arm and one further section for the forearm allowing horizontal movements in the elbow joint. The patients had to perform rhythmic alternating flexion and extension movements in the elbow joint. The rhythm was provided by a click tone stimulator. The spatial extent of movement was marked. Six manoeuvres (spatial extents of 48°, 83° at frequencies of 0.9 Hz, 1.5 Hz, 2.5 Hz each) had to be absolved. The potentiometer converted the horizontal movements of the forearm into a variable voltage. Patients were investigated without and during contralateral VIM stimulation.

Results: In 5 patients the spatial and temporal accuracy of the alternating forearm movements increased significantly after the stimulation had been switched on. In 1 patient the movement accuracy during the "on" and the "off" condition was not different.

Conclusion: Both parameters muscle timing and muscle energizing improved significantly during VIM stimulation suggesting that VIM stimulation may reduce ataxia in MS patients.

P886

Randomized double-blind evaluation of unilateral deep brain stimulation of the subthalamic nucleus

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Objective: To determine the effect of *unilateral* deep brain stimulation (DBS) of the subthalamic nucleus (STN) on contralateral, ipsilateral and axial features of Parkinson's disease (PD).

Background: Bilateral STN DBS can improve all cardinal features of PD. While a bilateral procedure for a bilateral disease appears appropriate, conceivably, a unilateral procedure may provide sufficient benefit in this asymmetric disease with a shorter operative procedure and potentially improved side effect profile. If, in particular, bilateral and axial symptoms respond to unilateral STN DBS, the need for a second procedure may be postponed or even eliminated in a subgroup of patients.

Methods: Thirty-two consecutive PD patients were evaluated 1–3 weeks before and 4 months after surgery in the medication 'off' and 'on' conditions while receiving ongoing chronic STN stimulation. Outcomes included UPDRS-III, AIMS and timed motor tests according to the CAPIT protocol. UPDRS-III and AIMS evaluations were video taped and randomized for scoring by a blinded rater. Non-parametric tests were used to compare differences between baseline scores and post-operative scores with stimulation on.

Results: In the medication 'off' state, UPDRS–III (minus rigidity) mean scores before surgery and after chronic STN stimulation were 39.8 and 27.2, respectively (32% improvement, $P < 0.00001$). Contralateral, ipsilateral and axial parkinsonian signs significantly improved with chronic unilateral STN stimulation. Total contralateral bradykinesia scores (items 23–26) improved from a mean of 9.0 to 6.0 ($P < 0.00001$). Total ipsilateral bradykinesia scores (items 23–26) changed from a mean of 7.3 to 6.3 ($P = 0.008$). The postural stability mean score improved from 1.2 to 0.7 ($P = 0.003$). Gait scores improved from a mean of 1.8 to 0.9 ($P < 0.00001$). The mean stand/walk/sit test score (unblinded) improved from 17.3 to 10.2 sec ($P < 0.00001$). In the best medication 'on' state, the mean total contralateral AIMS score improved from 4.8 to 3.2 ($P = 0.012$). Mean ipsilateral AIMS scores were 4.0 and 2.7 ($P = 0.013$). The mean levodopa equivalent dose was 31% lower after surgery. This reduction did not lead to aggravation of parkinsonian symptoms on the ipsilateral side.

Conclusion: Unilateral STN DBS was associated with clinically meaningful improvement. The combination of significant bilateral and axial improvement from chronic unilateral STN DBS demonstrates the utility of this procedure in advanced PD.

P887

Bilateral globus pallidus stimulation for Huntington's disease: Importance of frequency on the clinical benefit

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Objective: To investigate the effectiveness of globus pallidus (GP) deep brain stimulation (DBS) in improving movement disorders in Huntington's disease (HD).

Background: Medical treatment for the movement disorders of HD is often ineffective or poorly tolerated. Pallidotomy and human fetal striatal transplantation have shown variable clinical results. Because of the benefit induced by GP DBS in levodopa-induced dyskinesia and dystonia, we performed bilateral GP DBS in one patient with severe chorea due to HD.

Methods: A 42-year-old man with HD was selected for bilateral GP DBS because of the severity of chorea and the absence of severe depression and psychosis. Before surgery he also presented with severe speech, swallowing, gait and balance impairment. His Unified Huntington's Disease Rating Scale (UHDRS) motor assessment score was 86 (dystonia subtotal score was 16, chorea subtotal score was 25). Bilateral GP DBS was performed using Leksell's'frame and MRI imaging under local anesthesia. The positioning of the electrodes (Medtronic 3387) was determined using microrecording and micro- and macro-stimulation. A Kinetra pace-maker was implanted in his right subclavicular region one week later.

Results: Double blinded video-taped assessment performed 20 days and 8 months after surgery showed that, maintaining the total energy delivered constant, 130 Hz monopolar stimulation at contacts 2 and 6 induced generalized bradykinesia and suppression of chorea. A lower frequency of stimulation (40 Hz) improved chorea without worsening baseline bradykinesia. At 8-month follow-up his UHDRS motor score was 54 (37.2% improvement) with dystonia subtotal score 10 (37.5% improvement) and chorea subtotal score 11 (56% improvement).

Conclusion: GP DBS may allow control of chorea and dystonia in HD without worsening bradykinesia through the modulation of the electrical parameters of stimulation.

P888

Subthalamic nucleus deep brain stimulation is effective for disabling dyskinesia, but does not improve early morning painful dystonia in Parkinson's patients

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Objective: To analyze changes in dyskinesia and dystonia scores 6, 12 and 18 months after subthalamic nucleus deep brain stimulation surgery (DBS STN) in patients with idiopathic Parkinson's disease (PD), particularly in comparison with mean levodopa (LD) equivalent doses.

Background: DBS STN is known to reduce Unified Parkinson's Disease Rating Scale (UPDRS) total scores, individual subscores (part I-IV) as well as medication requirements in advanced PD up to 5 years after surgery. We studied the effect of DBS STN on dyskinesia and early morning dystonia. A comparison was made between dyskinesia, early morning dystonia, part IV UPDRS total scores and total medication requirements before and 6, 12 and 18 months after surgery.

Methods: DBS STN was carried out on 27 patients with advanced PD between 2000 and 2003 and data for all relevant variables was available in 18 (15 bilateral, 3 unilateral). All patients had disabling dyskinesia/or dystonia prior to surgery and all patients had been on dopaminergic medication immediately prior to surgery. Patients were assessed with total UPDRS pre-operatively and 6, 12 and 18 months post-operatively in the "ON" state (on medication, on stimulation). Subsections of part IV of the UPDRS were analyzed separately. These data included part IV A (question 32: dyskinesia duration, 33: dyskinesia disability, 34: dyskinesia pain, 35: early morning dystonia); IV B (clinical fluctuations); IV C (other complications); and total scores of part IV UPDRS (A+B+C). Patients were also assessed before and 6, 12 and 18 months after surgery for medication change, which was calculated as total LD equivalents.

Results: Dyskinesia duration, disability and pain (question 32–34) showed statistically significant reduction at 6, 12 and 18 months after surgery ($P < 0.05$). Early morning dystonia (question 35) showed no significant change at 6, 12 or 18 months after surgery. Total scores of part IV UPDRS revealed statistically significant decreases at 6, 12 and 18 months after surgery ($P < 0.05$). Mean UPDRS total scores and total LD equivalent showed a clear decreasing trend at 6, 12 and 18 months after surgery but did not reach statistically significant values. Daily LD equivalents were reduced by 7.7% at 6 months, 11.7% at 12 months and 19.3% at 18 months after surgery (Table 1).

Conclusion: STN DBS is safe and effective for treatment of disabling dyskinesia, but does not improve significantly painful early morning dystonia. All patients ($n = 18$) revealed statistically significant reductions in total scores of Part IV of the UPDRS up to 18 months after DBS STN. All dyskinesia scores remained significantly reduced at 6,12 and 18 months after surgery despite minimal reduction of medication at 6 month after DBS. Early morning dystonia was not improved. Our results support direct benefit from DBS STN on dyskinesia reduction rather than benefit due to medication reduction.

TABLE 1 (P888). *Percent decreases of LD doses and UPDRS ratings for patient group (n = 18)*

	Pre-surgery to 6 mo.	Pre-surgery to 12 mo.	Pre-surgery to 18 mo.
Daily LD equivalents	7.7	11.7	19.3
UPDRS Total score	18.5	24.4	11.6

P889

Subthalamic nucleus deep brain stimulation with or without microelectrode recording: Complications analysis in two groups

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Objective: To analyze the complications of patients receiving subthalamic nucleus-deep brain stimulation (STN-DBS) with or without intraoperative microelectrode recording (MER).

Background: The morbidity of stereotactic surgical complications in movement disorders was varied from 12–32%. We compared the complication rate of the patients in our institute who underwent STN-DBS with or without intra-operative MER.

Methods: From February, 2002 to December, 2003, thirty patients with movement disorder and intractable seizure underwent STN-DBS in our institute. The mean followed duration was 10.4 ± 7 months. They were divided into two groups for comparison. Group A (without MER) included 8 patients (mean age, 60.5 ± 10 year; male, 4; female, 4). In which, 16 intracranial procedures were performed and 8 batteries were implanted. Group B (with MER) included 22 patients (mean age, 54.6 ± 19 year; male, 13; female, 9). In which, 43 intracranial procedures were performed and 23 batteries were implanted.

Results: The overall intracranial morbidity was 8.4% (N = 4/30). Which included two electrodes mal-positioning occurred in group A (12.5%, N = 2/16), one in group B (2.3%, N = 1/43), and one asymptomatic intracerebral hemorrhage occurred in group B (2.3%, N = 1/43). The overall extracranial morbidity was 19.4% (N = 6/30). Which included one battery implantation site hematoma and two batteries migration in group A (37.5%, N = 3/8). In group B, two battery implantation sites hematoma and one effusion occurred (13%, N = 3/23). Other complications included: one seizure attack in group A (12.5%, N = 1/8); one eyelid opening apraxia occurred in both group A and B (12.5%, N = 1/8 vs. 4.3%, N = 1/22); two patients experienced DBS related hypo-maniac in group A versus three in group B (25%, N = 2/8 vs. 13.6%, N = 3/22). The overall mortality rate was 6.7% (N = 2/30), which were not surgical related.

Conclusion: The high morbidity in group A may be the learning curve of a new surgical technique.The use of MER should increase the accuracy of electrode implantation without increase the intracranial morbidity rate. The hypo-maniac state might be related to the site of electrode implantation inside the STN or the additive effect of DBS by dopaminergic therapy.

P890

Unusual observations following subthalamic nucleus stimulation

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Objective: To study the effects of subthalamic nucleus (STN) Deep Brain Stimulation (DBS) in patients suffering from Parkinson's disease

Material: Thirty-three patients underwent bilateral STN stimulation for PD at our institute between 1999–2002. The average follow-up has been 6 months. We observed certain stimulation related symptoms/side effects that have not been reported before. We observed severe depression, increased urinary frequency, hemiballism and isolated pseudo-bulbar symptoms. These symptoms were directly related to stimulation. Despite the symptomatology, the stimulation parameter were effective in obtaining improvement in Parkinson's disease as observed by reduction in the Unified Parkinson's Disease Rating Scale and levodopa dosage. We have postulated the hypothesis explaining these symptoms in the current presentation.

Conclusion: Apart from alleviating symptoms and signs of PD, the DBS electrodes set into motion a small electrical "storm" in a focal area of the brain namely the STN. This electrical field not only changes STN function but it can disturb surrounding areas leading to new "effects". This produces neurological symptoms some unpleasant requiring immediate attention, like depression. Changing electrical parameters could rectify all these problems. Therefore they are important to recognize.

P891

Conscious sedation versus local anaesthesia in deep brain stimulation surgery for Parkinson's disease

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Objective: To evaluate conscious sedation in Deep Brain Stimulation (DBS) surgery.

Background: DBS is an usual procedure in the treatment of different movement disorders, particularly Parkinson's disease. DBS is undertaken in two steps. Firstly, electrode target implantation, and secondly, internalisation of the stimulator. Electrode implantation is usually performed under local anaesthesia alone, which is very uncomfortable for the patient, or sometimes, under general anaesthesia, which may interfere with neurophysiological recordings and clinical evaluation. Conscious sedation constitutes a state of minimally depressed level of consciousness without affecting the ability of the patient to maintain airway reflexes, and to respond to physical exam or verbal commands. This technique provides a comfortable state to the patient during surgery and, importantly, amnesia of the surgical procedure, without interfering with the electrophysiological registry of neural activity.

Methods: Advanced Parkinson′s disease patients, selected for DBS.

Design: Single blind study, to compare conscious sedation vs. local anaestesia alone during electrode implantation; 20 patients were estimated to be evaluated in each arm. The assignment to each group was consecutive *Conscious sedation technique:* For electrode implantation, midazolam, 2 mg iv, are administrated five min before local anaesthetic infiltration. One minute before this infiltration, a bolus of propofol, 1 mg/kg, is given. A mixture bupivacaine, 0.33%, with epinephrine, diluted 1:200,000, is employed for local anaesthetic infiltration. It provides adequate scalp anaesthesia for 8–12 hr. The same scheme can be used during scalp suture. To assess patients' perioperative pain and amnesia we used a visual analogical scale (VAS). The evaluating physician was blind to the procedure. The neurophysiologist evaluates blindly the interference with neural recordings.

Results: An interim evaluation of the first 10 patients of each arm disclosed a significant benefit for patients treated with conscious sedation. There was no interference with neural recordings between both procedures. As a consequence, conscious sedation was the technique adopted since them; the following 20 patients were also evaluated to assess the consistency of the procedure. Data are shown in the tables.

Conclusion: Conscious sedation significantly improved perioperative pain and amnesia compared to local anaesthesia, without interfering with neural recordings.

TABLE 1 (P891). *Perioperative pain results*

	n	Med ± SD	Min-Max	p (95% CI)
Conscious sedation	10	3.14 ± 0.82	1.90–4.30	<0.0001 (2.62–4.97)
Local anaesthesia	10	6.94 ± 1.16	4.80–8.80	
Conscious sedation	30	3.44 ± 0.85	1.50–4.80	

TABLE 1 (P891). *Perioperative amnesia*

	n	Med ± SD	Min-Max	p (95% CI)
Conscious sedation	10	4.32 ± 1.12	2.90–6.20	<0.0001 (3.97–5.94)
Local anaesthesia	10	9.28 ± 0.64	8.20–10.0	
Conscious sedation	30	3.81 ± 1.86	2.70–6.20	

P892

Two-year follow-up of bilateral subthalamic nucleus stimulation in Parkinson's disease

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Aim: High frequency stimulation of subthalamic nucleus (STN) is known to ameliorate the signs and symptoms of Parkinson's disease. We report our experience with this therapy in 30 patients followed up over the period of 2 years in our hospital.

Methods: 30 patients suffering from severe Parkinson's disease (stages III-V on Hoehn and Yahr Scale) underwent bilateral implantation of the electrodes in the STN. Preoperative and postoperative assessments of these patients at 1 and 2 years of follow-up, in "On" and "Off" drug conditions while "On" stimulation, were carried out using Unified Parkinson's Disease Rating Scale (UPDRS), Hoehn&Yahr staging and Schwab and England Activities of Daily Living Scores alongwith video recordings.

Results: As compared with baseline ("Off" medications), the patients scores for activities of daily living and motor examination (UPDRS parts II and III) "Off" medications "On" stimulation, at 1 year improved by 62% and 61% respectively ($P < 0.005$). Corresponding improvement at 2 years was 61% and 58% respectively. There was no difference in the improvement in the activities of daily living and motor examination parts of the UPDRS at one year and two years "Off" medications "On" stimulation. The subscores for bradykinesia, rigidity, tremor, gait and dyskinesias also improved ($P < 0.005$). The average levodopa dose decreased from a mean of 774 mg preoperatively to 451 mg at 1 year of follow-up. However, the levodopa requirement increased to 531 mg at the end of 2 years. The cognitive functions remained unchanged. One patient underwent device explantation following infection related complications, one patient died of a cardiac arrest while one patient was lost to follow-up.

Conclusion: Patients with advanced Parkinson's disease treated by bilateral STN stimulation showed marked improvement in motor function "Off" medication "On" stimulation as compared to baseline "Off" medication. Reduction in levodopa dosage due to successful deep brain stimulation lead to reduced dyskinesias. There was no loss of efficacy at 2 years as compared to 1-year follow-up. However, there was a marginal increase in levodopa requirement at 2 years as compared to 1 year follow-up. This was not associated with any change in dyskinesias. We conclude that bilateral STN stimulation continues to be beneficial at the end of 2 years.

P893

Subthalamic nucleus stimulation for Parkinson's disease: Anatomical localization of the exact target

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Background: High frequency stimulation of the subthalamic nucleus (STN) has become a widely accepted therapy for patients with advanced Parkinson's Disease (PD). Despite the efficacy of "STN" stimulation, controversy continues over the exact target site: is it the STN itself, the Fields of Forel, the Zona Incerta, or a combination of these structures?

Objective: To anatomically localize the exact location of the active electrode contact and correlate it with clinical outcomes.

Design: The positions of the active contacts were identified on the stereotactic post operative radiographs and normalized to the ventriculographic 3rd ventricular landmarks. The same ventricular landmarks were then defined on the preoperative turbo spin echo MRI scans thus enabling superimposition of the exact location of each contact from the radiographs onto the MRI scans. The location of each contact was then verified in relation to the STN's dorsoventral, mediolateral, and anteroposterior axes. This technique rather than direct measurements on the post operative MRI scan was used as the latter is made inaccurate by the electrode artifacts. The relationship between contact position and clinical outcomes were then investigated by multiple regression analysis.

Subjects: 13 patients with idiopathic PD treated with bilateral STN implantations in whom the STN borders were identifiable on the preoperative MRI scans.

Outcome measures: Unified Parkinson's Disease Rating Scale (UPDRS) for tremor, rigidity and akinesia. Postoperative off medication/on stimulation scores were compared to the preoperative off medication scores.

Results: The average age of patients was 52 years with a post operative follow up of two years. All patients received monopolar stimulation through the most clinically efficacious contact (active contact) of a four-contact electrode. A total of 26 active contacts were analyzed. 23 of the active contacts were located inside the STN borders. The remaining 3 contacts were located just outside the medial border of the STN. The average contact position along the dorsoventral axis was 46.7% (SD 22.9) from the ventral pole. The average along the anteroposterior axis was 43.7% (SD 16.3) from the posterior pole and that in relation to the mediolateral axis was 67% (SD 48.0) of half the STN's width from the mid-STN point. The relationships between the clinical outcomes and active lead locations did not reach statistical significance. A weak relationship between rigidity and position along the mediolateral axis was present with the contacts located further from the mid-STN providing less clinical benefit ($P > 0.05$).

Conclusion: The average coordinates of all plotted active contacts were located near the center of the STN. Stimulation of the STN itself, rather than any adjacent structures, is responsible for the clinical benefits seen in PD.

P894

Neuronal activity of *zona incerta* in Parkinson's disease patients

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Objective: To describe firing characteristics of ZI in Parkinson's disease patients.

Background: A diencephalic structure dorsal to the subthalamic nucleus, the *zona incerta* (ZI) has been described as a relay station between the brain stem and higher centres. 6-ODH lesioned rats ZI proved to become hyperactive compared to normal rats, supporting previous reports of ZI being a putative target for surgical treatment of Parkinson's disease.

Methods: Twelve patients who underwent microrecording guided subthalamic surgery consented to the study, taking advantage of ZI being in the microrecording pathway for targeting the dorsolateral region of STN. Patients were awake during all recordings, according to the surgery protocol. Neurones from different tracts were classified as belonging to ZI according to their firing features, anatomical mapping of trajectories and atlas confirmation; they were then extracted and isolated from surgery recordings and analyzed offline (CED 1401 plus and Spike2 software). Only units that satisfied a minimum 2:1 signal to noise ratio were included.

Results: Sixty-eight neurones were classified as ZI. Mean firing rate proved to be 19.5 Hz. Pattern analysis showed heterogeneous neuronal signals ranging from tonic to burst and paused neurones, determining high dispersion values of the total population, leading to further analysis and sub-classification into different classes of firing patterns. Five of the recorded neurones showed a rhythmical oscillation in their spike trains from 8 to 14 Hz, characterised by repetitive bursts of 3 to 9 spikes (mean inter-spike interval of bursts 6.3 msec). Two units were found to discharge bursts (trains of 4 to 7 spikes, mean ISI 2.7 msec) at a 4-Hz tremor frequency in a phase locked manner. None of the recorded ZI neurones responded to proprioceptive manoeuvres.

Conclusion: ZI presents a distinctive and characteristic firing activity, easily differentiated from STN in Parkinson's disease patients. The firing rates found agree with those described as hyperactive in 6-OHD lesioned rats.

P895

A practical guide to deep brain stimulation in Parkinson's disease and other movement disorders

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Objective: To publish a document that could be used nationally to ensure appropriate specialist nursing care for patients undergoing functional neurosurgical procedures for movement disorders.

Background: Surgery for movement disorders is becoming increasingly common, not only in the UK, but also internationally. There is clearly a need for nurses to develop expertise in this field of neuroscience nursing in order that patients receive appropriate care delivered by skilled practitioners. When the first Surgical Movement Disorder Nurse Specialist was appointed in England in 1996 most patients, for whom functional neurosurgical procedures were appropriate, were undergoing lesional procedures for Parkinson's disease and tremor. Since that time, surgical techniques have developed and the majority of patients are now treated by implantation of deep brain stimulators. The range of movement disorders treated has also increased to include disorders such as dystonia, chorea, and other more unusual conditions. Until now, it has been difficult for specialist nurses, who are new in post, to access information about the management of deep brain stimulation systems and there are currently no nursing courses available to address this. There is therefore a need to provide appropriate information that is readily available in the clinical setting. The *Practical Guide* is designed as an A5 file with inserts so it can easily be carried around as needed.

Methods: A steering group was set up to undertake this project and to secure funding for the publication of the document. The document has been distributed at the Parkinson's Disease Nurse Specialist Association (PDNSA).

Conclusion: Medtronic Ltd, as the main supplier of neurostimulation devices, provide some training and support for specialist nurses in this field, but it is hoped that this publication will provide a valuable source of practical advice for nurses in the work place. It will also allow other healthcare professionals who are involved in the care of such patients to gain a greater understanding of this therapy and its implications for patients and their families.

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P896

Stimulation parameters' relationship to stimulation effect in deep brain stimulation of the thalamus

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Background: Electrical stimulation (DBS, deep brain stimulation) is an effective treatment for a number of movement disorders. The current generation of implantable pulse generators (IPGs) allows the clinician to adjust electrical parameters of the stimulation (frequency, voltage, and pulse width) to maximize benefit and minimize side effects. Establishing the quantitative relationship between electrical parameters and stimulation effect might make such adjustments more accurate or more efficient. In addition, it might provide insight into the mechanisms by which DBS acts.

Methods: We studied 9 patients (11 thalami) with essential tremor of the hands receiving DBS of the Vim nucleus of the thalamus. We randomly varied frequency, voltage, and pulse width, over the whole range of accessible values, subject to constraints of current density and subjects' comfort. We quantified tremor using 3-axis acelerometry of the contralateral hand.

Results: Pulse width proved to have little influence over tremor. Frequency and voltage, on the other hand, were highly influential, with complex interactions between the two. At low frequencies, tremor increased monotonically with increasing voltage. At high frequencies, the tremor-voltage curve was U-shaped. When viewed as a response surface [Box and Draper, 1987] this manifested itself as two ridges: in the low-frequency/high-voltage regime, a positive ridge, and, in the high-frequency/medium-voltage regime, a negative ridge. In addition, while the qualitative features of the response surface were uniform, it showed orderly variations across subjects. We constructed a simple mathematical model of DBS's effect based on two competing processes with different relations to stimulation frequency and voltage: tremor suppression and tremor aggravation. It proved able to reproduce the range of responses seen in our subjects, with a single fitted parameter allowed to vary between subjects.

Conclusion: We believe this supports the 'competing processes' conceptual model. In addition, it suggests that inter-subject variation is low-dimensional. This is consistent with the idea that inter-subject differences reflect differences in electrode placement. This is further supported by observations in one subject studied before and after surgical revision.

P897

Age is not an independent factor influencing the short-term outcome in parkinsonian patients treated with deep brain stimulation of the subthalamic nucleus

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Objective: To investigate the relation between age and the short-term outcome in parkinsonian patients treated with deep brain stimulation (DBS) of the subthalamic nucleus.

Background: Old age is thought to be confounding factor in the DBS surgery of Parkinson's disease because of declined cognitive function and impaired medical condition. The influence of old age itself in the DBS surgery is unknown.

Methods: Thirteen patients with Parkinson's disease whom treated with bilateral DBS of the subthalamic nucleus were studied. The thirteen patients were divided into the old (6 patients, mean age: 69.3) and the young (7 patients, mean age: 50) groups. We compared the short-term benefits (within the six months after surgery) of deep stimulation without levodopa (off medication) between the two groups, with using the Unified Parkinson's Disease Rating Scale (UPDRS). Other possible influencing factors were also compared between two groups in the study.

Results: The improvement of UPDRS score after DBS on (off medication) was better in the young group ($P < 0.05$). Before surgery, the improved UPDRS score with levodopa was also better in the young group ($P < 0.05$). The improvement with DBS (after surgery) and medication (before surgery) were compared in young and old group separately, but these were insignificant (for all comparisons). Other possible influencing factors (clinical stage, mini-mental status examination, disease duration, dosage of levodpa) were compared but insignificant.

Conclusion: The short-term benefits of bilateral DBS of the subthalamic nucleus are better in the young group in our study. This result may reflect the better medication improvement in the young group before surgery. Age is not an independent factor influencing the short-term outcome in parkinsonian patients treated with DBS of the subthalamic nucleus.

P898

How is the impedance of electrodes used for microelectrode recording related to the outcome of deep brain stimulation surgery for Parkinson's disease?

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Objective: To assess the relationship between impedances of electrodes used during microelectrode (ME) recording for deep brain stimulation (DBS) surgery for Parkinson's Disease (PD) and the final position of the chronic stimulating electrodes as well as clinical outcome of patients.

Background: Impedances of MEs are known to change after use, especially if they are also utilised for stimulation. MEs are often reused during bilateral DBS operations. There is a concern about the clinical sequel of this alteration in impedance.

Methods: This is a prospective study of 30 consecutive patients (16 males and 14 females) undergoing simultaneous five-channel ME recording during DBS of the subthalamic nucleus for PD. The procedures were bilateral and performed consecutively during one operative session with MEs reused for the same patients. MEs impedances were measured at the start of intracerebral implantation for each side of the brain. The choice of final ME track used for the placement of the chronic stimulating electrode was also noted. Patients outcomes were assessed by Unified Parkinson's Disease Rating Scale (UPDRS) for tremor, rigidity and akinesia at one year and compared to the pre-operative state. Scores for each side of the body were analysed separately for preoperative off drug versus postoperative off drug/on stimulation, and preoperative on drug versus postoperative on

drug/on stimulation conditions. The Outcome measures of interest were: The mean ME impedances; correlations and significance levels between the impedance and: 1, position of final chronic electrode, 2, clinical outcome scores; the difference in outcomes between the first and second operated sides.

Results: The mean age at operation and the duration of PD were 55.2 (SD = 9.9) and 13.2 (SD = 4.4) years respectively. The mean ME impedance at the start of surgery was 0.51 MΩ (SD = 0.25). This decreased to 0.14 MΩ (SD = 0.08) when electrodes were reused for the second side ($P < 0.000001$). Only for the initially operated side, was there a significant correlation between ME impedance and the choice of the chronic electrode track ($P = 0.04$ vs. $P = 0.24$ for the first and second sides respectively). In neither case was there a significant correlation between the impedances and the outcome of patients ($0.14 \leq P \leq 0.93$). Furthermore, there were no significant differences in the percentage improvement in outcome scores between the two sides of the body following surgery ($0.19 \leq P \leq 0.88$). The overall ratio for improvements between the sides of the body contralateral to the initially and the second operated sides of the brain was 0.93 compared to the theoretical ratio of one.

Conclusion: Microelectrodes with higher impedances may present better discriminatory properties when used for targeting in DBS surgery although the clinical relevance remains uncertain. Similarity of outcomes between the two operated sides serves to reassure concerns about patient and surgeon factors with lengthy bilateral operations.

P899

Retrospective comparison of the efficacy and costs of STN-DBS and continuous subcutaneous infusion of apomorphine in patients with advanced Parkinson's disease

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Objective: To compare retrospectively the efficacy of STN-DBS and subcutaneous infusion of apomorphine in patients with advanced PD, and also to calculate the direct costs of both treatments.

Background: STN-DBS has proven to be a very effective therapy for patients with advanced PD. However, many PD patients do not fulfill the inclusion criteria for STN-DBS and the capacity is limited. Apomorphine infusion therapy seems to be a real alternative, but good comparative data are lacking.

Methods: A literature search was performed to select all publications on either STN-DBS or subcutaneous infusion of apomorphine in PD. The articles were analysed looking for data on: off-time reduction, dyskinesia frequency and L-DOPA equivalent dose (LED) reduction. Finally, based on the Dutch situation, the direct costs of both treatments were calculated.

Results: Thirty-one studies on STN-DBS were found and 20 articles on infusion therapy with apomorphine. Only 5 STN-DBS studies reported data on all 3 endpoints, whereas 16 publications on apomorphine infusion reported data on off-time reduction and LED reduction. However, only 4 apomorphine publications reported on all 3 endpoints. The 5 STN-DBS studies showed an off-time reduction of 61–90% (mean 75%) vs. 50–85% (mean 62%) of the apomorphine infusion studies. The frequency of dyskinesia after STN-DBS was reduced by 39–86% (mean 70%) vs. 0–85% (mean 48%) in the infusion studies with apomorphine. The LED reduction in the STN-DBS groups varied from 22–80% (mean 47%) vs. −15–80% (mean 46%). The direct costs of 1-year treatment with a mean daily dose of apomorphine are 10,000 Euro, increased by an external pump (2,000 Euro) and catheters and syringes (2,500 Euro). Presuming the pump has a writing-off period of 4 years. the total costs of apomorphine infusion are 13,000 Euro/year. The costs of a STN-DBS procedure in the Netherlands reach a total of 28,000 Euro (surgery 13,000 Euro, Kinetra 11,000 Euro, electrodes 3,000 Euro, patient controller 1,000 Euro). The mean battery life of a Kinetra is about 5 years. If patients would use the same electrodes and patient controller for a mean period of 5 years, including the repositions and technical problems, the total direct costs of STN-DBS are 5,600 Euro/year.

Conclusion: The efficacy data of apomorphine infusion and STN-DBS show a large variance with considerable overlap. Both therapies show a very potent effect on off-time reduction, dyskinesia- and LED reduction. However, this analysis shows that both therapies are monitored very different, resulting in a restricted nr. of studies suitable for comparison. The yearly costs of apomorphine infusion are double the STN-DBS costs per year. However, apomorphine infusion seems to offer an almost equally effective alternative for all patients who fear a STN-DBS procedure or do not fulfill the strict inclusion criteria for STN surgery. Future studies have to investigate if the costs of apomorphine infusion outweigh the savings in terms of nursinghome admission, decreased nr. of hospital admissions, etc. A prospective well-designed comparative study will be needed to solve the issues mentioned above.

P900

Pallidal stimulation to treat tardive dyskinesia: Preliminary report of the French multicentric study STARDYS

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Objective: To assess the efficacy and safety of bilateral pallidal stimulation to treat severe neuroleptic-induced tardive dyskinesia (TD).

Background: TD is often a troublesome disorder with limited therapeutic possibilities. In view of the efficacy of pallidal stimulation in the treatment of L-DOPA-induced dyskinesia and idiopathic dystonia, we assessed the effect of this technique on TD.

Methods: Six patients (age = 47 ± 5 years) were included in the study. All of them suffered from disabling TD despite attempts of treatment with clozapine or tetrabenazine. The severity of TD was determined by means of a "TD score", a composite score calculated from the Extrapyramidal Symptoms Rating Scale (i.e., sum of the scores on the tardive chorea and tardive dystonia subscales). The mean TD score was 47 ± 10 (/106) at inclusion. There was a broad spectrum of symptoms: axial dystonia (4 cases) with buccofacial dyskinesia (2 cases); lower limb dystonia and upper limb chorea (1 case); upper limb chorea and buccofacial dyskinesia (1 case). Leads were implanted bilaterally in the internal part of the globus pallidus by stereotaxic surgery with targeting based on MRI and microrecordings.

Results: A clear improvement was obtained in all the patients after a few days of monopolar stimulation (voltage = 3.5 ± 0.3). The TD score had decreased by 55% [range = 30–80%] after 3 months of stimulation ($P < 0.05$). A similar improvement was obtained for both dystonia (62%; range = 0–80%) and chorea (60%; range = 30–90%). None of the patients had any permanent side effects and in particular there were no changes in their psychiatric state.

Conclusion: Despite being preliminary (the full study is designed to include 20 patients who will be followed up for one year), these results suggest that bilateral pallidal stimulation could be an effective and safe treatment for disabling TD.

P901

Cognitive, motor and quality of life outcomes after subthalamic stimulation for Parkinson's disease

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Objective: To describe the outcomes of bilateral subthalamic nucleus (STN) deep brain stimulation (DBS) in a consecutive series of patients with advanced Parkinson's disease (PD) who underwent comprehensive cognitive, motor and quality of life (QOL) assessments.

Background: Bilateral STN DBS is an effective treatment for selected patients with PD in whom disabling motor fluctuations and dyskinesia do not respond to standard pharmacological therapy. Most centers report significant improvement in Unified Parkinson's Disease Rating Scale (UPDRS) scores. Previous studies have reported somewhat variable cognitive outcomes. Few studies of STN DBS have measured quality of life outcomes.

Methods: Pre-op and 6 month post-operative "on" and "off" UPDRS scores, quality of life using PDQL [Hobson, 1999] and neuropsychological testing were compared for 20 patients undergoing bilateral STN DBS. The PDQL questionnaire measured parkinsonian and systemic symptoms and

social and emotional functioning. Cognitive assessment was carried out in the on-medication state before surgery, and in the on-stimulation, on-medication state post-operatively. The neuropsychological test battery included measures of general intelligence, attention and concentration, language, learning and memory, visual perception, frontal function, personality and mood. Microelectrode-guided intra-operative subcortical mapping allowed precise localization of the sensorimotor portion of the STN. STN activity was characterized by a region of at least 4-mm of high-amplitude spikes, the presence of kinesthetic responses to contralateral passive limb movements and occasional tremor-related activity. Statistical analyses were performed by way of repeated measures of analysis of variance. Alpha was set to 0.05.

Results: Pre-operatively, all patients demonstrated levodopa-responsiveness, good general health and were not demented. Complications of DBS implantation included a single post-operative seizure in two patients and one patient with an infection. After DBS programming two patients had worsened hypophonia and one had apraxia of eyelid opening. Post-operative UPDRS "off" scores for activities of daily living (ADL), total motor, axial motor, bradykinesia and tremor improved significantly, as did dyskinesia rating scores. Total PDQL scores as well subscores for parkinsonian, systemic and emotional functioning were also significantly improved, but subscores for social functioning were not. Neuropsychological assessment revealed that the only significant post-operative change in cognition was a mild decline in verbal fluency.

Conclusion: In this cohort of patients enhancement of QOL paralleled motor and ADL improvements following bilateral STN DBS. Comprehensive neuropsychological assessment revealed no evidence of cognitive decline. While some authors have reported declines in verbal and phonemic fluency, verbal memory and in the visuospatial domain, our patients showed only a mild decline in verbal fluency, supporting the lack of adverse cognitive effects of bilateral STN DBS in non-demented patients.

P902

Life-threatening non motor fluctuations: An emergency indication for sub-thalamic nucleus (STN) deep brain stimulation (DBS)

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Objective: To evaluate the effect of STN DBS on life threatening non motor fluctuations (NMF) in a Parkinsonian patient with dopaminergic psychosis.

Background: NMF are frequent and disabling manifestations in Parkinson's disease (PD). They can be extremely incapacitating specially dysautonomic or psychic fluctuations. STN stimulation is an effective treatment of motor and nonmotor fluctuations. We report here the case of a PD patient with life threatening NMF who underwent bilateral STN stimulation.

Methods: Motor function (UPDRS III) cognitive function (MMSE), psychic function (Beck Depression Inventory), psychiatric follow-up and quality of life were evaluated before and after (6 and 12 months) STN surgery on a patient with PD presenting with dopaminergic psychosis and severe NMF.

Results: A 55-year-old male with Parkinson's disease (disease duration: 10years) was hospitalized for severe fluctuations. After 8 years of benign evolution, he developed severe motor fluctuations associated with dopaminergic psychosis, which required institutionalization. At admission, he presented with severe off manifestations: complete dysphagia, dyspnea requiring oxygene therapy, extreme variations of the blood pressure, panic attack and delusions. Clozapine only partially alleviated psychosis but dopaminergic reduction intensified NMF. He still had a good motor response to L-DOPA (UPDRS III off: 42 / on:11). Although he did not meet the complete criteria for STN DBS, he was proposed for bilateral STN implantation as a life saving indication. After 1 year of chronic STN stimulation, his motor score improved by 67% and his L-DOPA daily doses were decreased by 83%. He had no motor fluctuations. His severe dysautonomic or psychic fluctuations also disappeared. His psychosis decreased and clozapine was reduced by 70%. He was able to return to his home and live with his wife. However, his cognitive functions worsened (presurgical MMSE: 21/Postsurgical MMSE: 15).

Conclusion: STN DBS is an effective treatment for life-threatening NMF. Although this patient had severe dopaminergic psychosis, STN stimulation did not worsen his behavioral disorder. It probably revealed an underlying dementia, which was compatible with a family life.

P903

Do changes in deep brain stimulation parameters affect mood and mental function in patients with Parkinson's disease?

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Objective: To examine whether PD patients treated with DBS experience changes in mood and cognitive function in association with changes in stimulator parameters

Background: DBS has been shown to improve motor symptoms with either STN or GPi stimulation. Cognitive and mood changes have been examined, mainly by comparing baseline measures to those obtained between 3–24 months after initiation of DBS. Several case reports suggest that DBS is occasionally associated with dramatic changes in mood. While these studies raise the possibility that DBS may be associated with subtle changes in cognition and mood, the relative contribution of stimulation compared with changes in medication, PD progression or other factors is difficult to determine. Another approach to address these issues is to examine whether behaviour changes as a function of stimulation parameters, i.e., whether it is on or off, or as a function of different stimulator settings.

Methods: We examined 20 IPD patients during device programming, assessing their mood, mental and motor function during each setting used in the effort to optimise their motor function. Patients were off medication (average: 8 hr before the testing session). During each stimulator setting, patients were requested to complete 3 simple linear rating scales, one for mood, one for mental function, and one for motor function. The person programming the device (experienced in assessing motor function) was also asked to complete the motor scale (mobility score-MbS-) after evaluating the patients' motor ability. In order to minimize potential confounding effects of mood/mental function changes with the patient's perception of motor change, the scales on mood and mental functions were administered a few minutes after the change in the stimulator parameters but before the patient attempted to move. MbS scale was administered after the mobility test. We compared the ratings of mood/mental function with the stimulator turned off (14 patients) to those with both the stimulator on and at the worst MbS and with stimulator on at the best MbS. We also directly compared the mood/mental function ratings at the worst MbS to those at the best MbS.

Results: There was a significant difference both in mood and mental function ratings between the best and worst MbS ($P < 0.01$), suggesting that patients feel more alert and in a better mood when the stimulator setting is improving their mobility. There was also a significant difference in mood between the stimulator off condition and the best MbS stimulator on condition ($p = .01$). For mental function, there was a positive trend ($P = 0.06$). We did not find any differences related to stimulator site (STN or GPi) nor brain side.

Conclusion: Our findings suggest that changes in stimulation parameters can be associated with improvement in mood and mental function in conditions in which motor function is also improved. To what extent these changes are independent of motor function is an issue requiring future research. However, the present findings underline that it is important to consider the possibility of influencing these behavioural areas when programming the DBS device.

P904

Bilateral chronic high frequency subthalamic stimulation in Parkinson's disease: Long-term neurological follow-up

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Objective: To describe the long-term results of subthalamic nucleus (STN) high frequency stimulation (HFS) for Parkinson's disease (PD).

Background: STN-HFS is a robust new symptomatic treatment for PD. The first available long-term observations show the stability of the efficacy of this procedure in time.

Methods: Quadripolar leads were implanted bilaterally under stereotactic conditions in the STN of advanced PD patients. Following implant, antiparkinsonian medication was reduced as much as possible and stimulation was gradually increased. The patients were evaluated in the practically defined "off" condition and in the "on" condition using the unified PD rating scale (UPDRS). Neuropsychological testing was performed before and after the implant. The present series deals with 40 consecutive patients followed at least for 12 months after STN-DBS; 8 among them until 60 months.

Results: Patients' mean age was 55.7 ± 7.7 years and their mean disease duration was 11.9 ± 4.2 years; they were followed-up for an average of 25.4 ± 16.7 months. At the time of the last visit, levodopa-equivalent daily dose was reduced by 56.2% ($P < 0.001$). Parkinsonian features were improved in all patients, the greatest changes were seen for tremor, gait, bradykinesia and postural stability, then rigidity and limb akinesia. Compared with the pre-implant conditions, the UPDRS motor score in the "off" condition was improved by 38.2% at the time of the last visit ($P < 0.001$). The neuropsychological data did not show significant changes. Night sleep improved in all patients. The most common permanent side effects consisted in hypophonia and dysarthria, transient side effects were increased sexuality and mania, the most common side effects related to stimulation were ballic or choreic dyskinesias. The most common adverse event related to the surgical procedure was transient psychosis; unexplained switching-off of the stimulator was the most common device-related effect.

Conclusion: This study confirms again that symptomatic efficacy of STN-HFS is retained at least during the first 5 years following the implant, without any obvious decay of efficacy. Improvement of dyskinesias also persists. Side effects and adverse events are sometimes severe, but can be managed in most cases. The improvement of patients' lifestyle outweighs by far the motor benefit. Bilateral STN-HFS is a relatively safe procedure, as regards the long-term cognitive and behavioural morbidity. Patients with young-onset Parkinson's disease suffering from levodopa-induced motor complications, who have sustained response to levodopa and exhibit no behavioral, mood, or cognitive impairment, benefit the most from STN-HFS. In patients who respond to L-DOPA, but have intolerable adverse effects, STN-HFS allows to decrease medication dosages (up to complete withdrawal in selected cases). Continuous STN-HFS is a robust treatment for advanced PD. Careful patient selection is mandatory to obtain the best clinical results. The precision of the targeting and the quality of the postoperative follow-up are the other main determinants of success of this surgical procedure.

P905

Management of hemidystonia with deep brain stimulation

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Deep brain stimulation (DBS) is an alternative for the treatment of dystonia, especially when the medical approach fails and the patient has significant disability. The usefullness of the procedure has been demonstrated in Primary Idiopathic Dystonia, Cervical Idiopathic Dystonia and Hemidystonia. In the first two cases a bilateral procedure is mandatory but in the last one, a unilateral DBS contralateral to the affected side of the body is done. The best results of functional surgery usually occur in primary dystonia.

A number of series had observed an improvement between 34–79% when the Internal Globus Pallidus (GPi) is the surgical target and 30–70% when the thalamic ventral Intermedius nucleus (VIM) is elected. The axial symptoms respond better to the stimulation of the GPI.

A 18 year old male with severe right hemidystonia is presented. His symptoms began in early childhood with slow progression, interfering with his normal activities. As a result of his disabling dystonic symptoms he had to retire the school when being 15 year old. The neuroimages and metabolic test did not show abnormalities and the cognitive performance was normal. The patient received medical treatment with anticholinergics, levodopa and benzodiazepines without improvement and then was considered a surgical candidate. Initially a stereotaxic lesion of the left GPI was performed with improvement of the symptoms only for three months. For these reason a decision to carry on a new surgery with DBS was taken. The procedure was performed without complications. The patient had a good improvement with a reduction on the Burke-Fahn-Marsden dystonia scale from 76–16 and now has been able to return to school and initiate a rehabilitation program.

P906

Surgical management of Parkinson's disease. Deep brain stimulation of the prelemniscal radiations

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The surgical approach to Parkinson's disease (EP) treatment has had significant advances over the last 20 years and is now an alternative for the management of advanced disease. There are several surgical targets to choose according to the patient and the predominant symptoms or complications (dyskinesias and motor fluctuations). Lesion surgery and deep brain stimulation (DBS) are the available surgical technics. The DBS has some advantages (no definitive lesion, modulation of the stimulators to improve the patients), but is very expensive in relation to ablation surgery.

The targets that had been used to treat EP are: Internal Globus Pallidus: improves levodopa-induced dysquinesias; Subthalamic nucleus: improves the cardinal symptoms of EP and disquinesias; Ventral Intermediate nucleus of Thalamus: improves tremor; Prelemniscal Radiations: improve tremor and rigidity.

The stimulation of the Prelemniscal Radiations is a newer, safe and efficient method, with few side effects because it affects a tissue zone without cells.

A 65-year-old male with a 8 year history of PD (Hoehn&Yahr IV) is presented. The predominant symptoms were tremor and rigidity, with an initial good response to levodopa. Over the course of 6 years his motor response became short lived and the patient was very disabled in his daily activities. No significant dyskinesias were observed and his cognitive performance was normal. Because of little improvements with different medical therapies, a decision to a surgical procedure was taked. The selected target was the prelemniscal radiations, according to the main symptoms. The procedure was performed without complications. Once the stimulators were programmed, the patient had a significant improvement with a reduction of 40% in the UPDRS parts II and III.

DBS of Prelemniscal Radiations offers a new avenue for the treatment of advanced PD, particularly for patients affected by severe tremor and rigidity resistant to medical therapy.

P907

Neuropsychological outcome of the deep brain stimulation of the subthalamic nucleus in patients with Parkinson's disease

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Objective: To investigate whether deep brain stimulation (DBS) of the subthalamic nucleus (STN) affects neuropsychological functioning in patients with Parkinson's disease.

Background: The cognitive effect of the new therapeutic procedure of STN DBS has been studied beside its motor effects. Some studies reported possible negative effects and some studies reveals the STN DBS did not affect memory or executive functions.

Methods: Ten patients with Parkinson's disease who underwent bilateral DBS of the STN were assessed with comprehensive neuropsychological tests before and 6 months after the surgery. To cover the domain of intelligence, memory, attention, and frontal function, the following tests were employed: 1 Mini-mental state examination, 2 VIQ of the Wechsler Adult Intelligence Scale-Revised (WAIS-R), 3 PIQ of the WAIS-R, 4 Verbal Memory Quotient (MQ) of the Wechsler Memory Scale-Revised (WMS-R), 5 Visual MQ of the WMS-R, 6 Digit span, 7 Spatial (Tapping) span, 8 Word fluency of category, 9 Word fluency of letters, 10 Trail Making Test B-A, 11 the number of categories achieved on the Wisconsin Card Sorting Test, 12 Stroop test, and 13 Tower of Hanoi. We used T-test

to compare the scores on these tests before the surgery with those after the surgery.

Results: No significant differences were found between the scores before and after the surgery ($P < 0.05$).

Conclusion: The DBS of the STN does not impair the patients' performance, as far as the tests we employed are concerned.

P908

Relief of hemiballism with ventral subthalamic stimulation following subthalamic nucleus deep brain stimulator implantation

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Objective: To describe a Parkinson's disease (PD) patient for whom delayed post-operative hemiballism following bilateral subthalamic nucleus (STN) deep brain stimulating electrode implantation was controlled with contralateral STN deep brain stimulation (DBS).

Background: Hemiballism is a rare disorder characterized by unilateral, wide-amplitude, often proximal uncontrolled movements. Long associated with lesions of the STN in non-parkinsonian humans, lesions outside the STN may also cause it. PD confers some protection from hemiballism in humans. Thalamotomy, thalamic DBS and pallidotomy can alleviate hemiballism, but there have been no reports of STN DBS improving hemiballism.

Case Report: A 63-year-old woman with advanced PD causing severe motor fluctuations and dyskinesia underwent implantation of bilateral STN DBS electrodes. Pre-operative UPDRS total motor score was 66 "off" medication, improving to 29 "on" medication. Intraoperative micro-electrode mapping revealed 6 mm extent of STN on the right and 7 mm on the left. There were no complications. Initial programming of both stimulators four weeks after surgery produced outstanding improvement. PD medications were continued. Two weeks later the patient reported complete relief of on/off fluctuations and dyskinesia. "Off" total motor score was 19. Seven days later she reported an inadvertant turn-off of both IPGs at a store entrance. Following that she reported increasing severe right sided dyskinesia. Reduction of bilateral DBS amplitude and of PD medication did not help. Amantadine provided no relief. The right-sided movements worsened. Both pulse generators were turned off and all PD medication except amantadine was discontinued. When examined 4 days later she required hospitalization for right hemiballism. Examination showed relief of right-sided PD signs and slight rigidity and bradykinesia on the left side. There were no other abnormal findings. Reprogramming of the left electrode worsened the hemiballism when the previous contact (located in dorsal STN) was used. Stimulation with a more dorsal contact in the region of zona incerta did not help. Stimulation with the adjacent contact in the ventral STN produced immediate cessation of hemiballism. MRI revealed a small hemorrhage limited to the left STN. Bilateral DBS was continued; the patient was discharged home on amantadine with both DBS stimulators turned on. Follow-up at 2 weeks revealed no recurrence of hemiballism.

Conclusion: Both delayed hemorrhage following DBS and hemiballism following neurosurgical procedures for PD are very rare. In our patient the small hemorrhage produced hemiballism as well as marked relief of contralateral parkinsonism. While hemiballism usually resolves weeks to months after onset, we observed a dramatic and immediate cessation with DBS reprogramming. Although hemiballism has occurred only rarely after STN DBS, it has been reported in several PD patients following subthalamotomy. The mechanism of hemiballism following STN injury in PD is unclear and may involve reciprocal connections of STN with the external and internal globus pallidus.

P909

Pathological crying induced by deep brain stimulation: A case report

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Objective: We present the case of a patient with Parkinson's Disease (PD) who developed pathological crying (PLC) during chronic deep brain stimulation (DBS) three years after bilateral implantation of electrodes in the subthalamic nucleus (STN). Clinical data as well as the exact localisation of the stimulation pole were analysed and a PET activation study was performed to characterise the mechanisms of this psychomotor phenomenon.

Background: High frequency DBS of the STN has become an effective surgical treatment for PD improving all cardinal motor symptoms by affecting striato-thalamo pathways to motor cortices. The STN is also known to be interconnected with limbic and prefrontal associative areas. Clinical observations of STN-DBS reported emotional effects like acute depression, acute episodes of laughter, relief from depression as well as changes in executive and memory functions. These findings have been characterised by analysis of stimulation pole localisation and functional PET imaging. However, pathological crying, a phenomenon of incontinence of affect, induced by DBS has never been reported so far. A recent theory suggests that PLC is caused by a disruption of higher association areas (that are involved in the adjustment of emotional responses according to a specific social context) from the cerebellum which computes profiles of emotional responses.

Methods: A 68-year-old patient with PD who reported episodes of crying without feeling sad three years after bilateral implantation of electrodes in the STN was examined. Stimulation sites were randomised under blinded conditions during a standardised interview to elaborate stimulation sites leading to PLC. CT and MRI scans were done to identify the exact electrode localisation. Finally butanol-PET was performed during different conditions: no stimulation and stimulation at two different sites located within the right STN.

Results: The patient only showed episodes of pathological crying when stimulation was set on. The phenomenon was more evident while stimulating the right hemisphere and at stimulation poles located within the STN. PET data gave evidence for stimulation induced activation of the ipsilateral thalamus, the ipsilateral pons and the contralateral cerebellum.

Conclusion: This is the first report of pathological crying (PLC) induced by subthalamic deep brain stimulation. Our data support the hypothesis that the cerebellum plays a crucial modulating role in the generation of PLC. In the present case STN-DBS probably triggers PLC by affecting thalamo-ponto-cerebellar pathways.

P910

Most effectrive stimulation site for severe intention tremor

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Objective: To evaluate the optimal target for intention tremor in thalamic deep brain stimulation

Background: DBS of the thalamic ventral intermedius nucleus (Vim-DBS) is an established therapy for patients suffering from severe, otherwise intractable tremor. It is considered particularly useful for patients with a disabling intention component in ET and MS. The efficacy of Vim-DBS has been demonstrated in several studies. However, the optimal stimulation site for severe intention tremor is still a matter of debate. Furthermore, it is unclear whether Vim-DBS exerts its beneficial effect by primarily influencing neurons within the Vim proper or adjacent fibre tracts.

Methods: We studied 7 patients with ET and 6 patients with MS following implantation of stimulation electrodes for Vim-DBS. We analyzed the localization of the contacts of the quadripolar electrode (Medtronic, model 3387) on stereotactic X-ray images. Based on intraoperative recordings we determined the position of the contacts relative to the ventral border of the Vim and the dorsal border of the subthalamic nucleus (STN). Three months after surgery, we evaluated the efficacy of each contact by assessment of a lateralized Fahn-score as well as analysis of accelerometry and grasping movements using a magnetic tracking system. We determined the chronaxie of the efficacious contacts for antitremor effect and stimulation-induced ataxia.

Results: Most efficacious contacts were located below the ACPC-line. Mean coordinates (mm relative to the midACPC) for the efficacious contacts were on the right side (x, y, z): 12.9 ± 1.6, -7.4 ± 1.0; -1.6 ± 1.3 and on the left side: -12.3 ± 1.2, -7.3 ± 1.7, -2.6 ± 1.1. Correlation of the position of the efficacious contact with intraoperative microrecording revealed localization between the ventral Vim border and the dorsal

STN border. Stimulation of contacts below ACPC-line led to a mean reduction of the lateralized Fahn-score by 63.6 ± 21.1% on the right side and 67.9 ± 18.3% on the left side. Stimulation of contacts above ACPC-line had a less marked effect with a reduction of 20.5 ± 16.4% and 17.6 ± 16.2%, respectively. All patients had a high amplitude wing-beating tremor in the off stimulation condition with an accelerometer total power [log $(mg^2)/(V^2)$] of 4.5×10^2 for the right side and 5.9×10^2 for the left side. Stimulation of contacts below ACPC-line led to a pronounced reduction of power to 2.5×10^1 and 3.4×10^0, respectively. Stimulation above ACPC-line had little or none effect on accelerometer power. Tracking of grasping movements showed a marked reduction of intentional tremor by stimulation of contacts below but not above ACPC-line.Determination of chronaxie in efficacious contacts revealed mean values of 27 ± 14 μs (mean ± SD) for suppression of tremor and 52 ± 15 μs for induction of ataxia ($P < 0.05$, t-test).

Conclusion: Based on clinical and electrophysiological evaluation, this study demonstrates that the optimal target point for alleviating severe intention tremor of ET and MS is located in the area below the thalamus and not within the Vim proper. Chronaxie values argue for an interaction with large myelinated fibres running in the subthalamic white matter.

P911

Bilateral pallidal stimulation in medically refractory tardive cervical dystonia: A case report

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Objective: To assess the response of bilateral deep brain stimulation of the globus pallidus internus (GPI-DBS) in a patient with medically refractory tardive cervical dystonia.

Background: Tardive dystonia is a disabling side effect associated with the long-term use of neuroleptic drugs and the medical treatment is usually difficult and often unsuccessful. Within the past few years, GPI-DBS has emerged as a significant therapeutic alternative in intractable primary dystonia. However, data for efficacy and safety in secondary dystonia are lacking. Only few cases of tardive dystonia have been treated with GPI-DBS and reported outcomes have been variable.

Methods: We report on a 59 year old male who developed tardive cervical dystonia following treatment with haloperidol for several years. He was treated with multiple medication including tetrabenazine, trihexyphenidyl, benzodiazepines, amantadine, tiapride, and repetitive botulinum toxin A + B injections without effect. Four years after onset of tardive dystonia GPI-DBS was considered. At baseline, the patient showed marked rotation and retroflexion of the head with continuous phasic head movements and elevation of the right shoulder (Tsui-score = 14). The patient underwent staged bilateral GPI-DBS under stereotactic conditions under local respectively general anesthesia using computed tomography and magnetic resonance imaging scans as well as ventriculography and microelectrode recording.

Results: Three months after surgery, chronic bilateral GPI-DBS resulted in a >80% improvement of tardive cervical dystonia with a Tsui-score of 2 (see video). Except for a mild non-disabling postural tremor and a weight gain of 5 kg no side-effects were observed.

Discussion: Bilateral GPI-DBS was safe and effective in a patient with severe medically refractory tardive cervical dystonia. Controlled trials are needed to establish the efficacy and safety of pallidal stimulation for medically intractable tardive dystonia.

P912

Side effects of subthalamic nuclei deep brain stimulation in Parkinson's disease: A retrospective study of 25 patients treated between 1998 and 2003

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Objective: To study medical and surgical side-effects of subthalamic nuclei stimulation in Parkinson's disease.

Background: Large series of patients have yet been published with emphasis on motor outcome and sometimes technical troubleshootings ; however, few have focused on medical and surgical side effects that can have dramatic impact on patients' quality of life.

Methods: We conducted a retrospective file study of the 25 patients operated on at our institution and looked for the side effects commonly described in the literature

Results: We had 3 intracerebral hemorrhage, with one subsequent death, 2 became aphonic when simulated, 1 became psychotic and had to be institutionalized; 3 electrodes out of 49 had to be replaced because of lack of efficacy; other less severe side effects will be further discussed.

Conclusion: Our data suggest that deep brain stimulation is an efficient treatment of advanced Parkinson's disease. However, side effects may affect the outcome of a minority of patients, sometimes seriously.

P913

Is the neurophysiological intraoperatory monitoring giving a better outcome in DBS therapy for Parkinson's disease? Our experience in 31 patients

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Objective: To investigate the efficacy of the neurophysiological monitoring on the clinical outcome of the Parkinson's disease patients treated with deep brain stimulation (DBS) of the subthalamic nucleus (STN).

Background: It is not globally accepted that the neurophysiology (microlectrodes recording and stimulation) is a useful tool in better localizing the STN. That is mainly because it is considered a time consuming and risky technique that doesn't add anything in accuracy to the very reliable neuroimaging methods.

Methods: Since 1998, 31 patients underwent bilateral NST implanting for an advanced phase of Parkinson's disease (HY score ≥3). We have had the opportunity to compare the results observed in 14 patients (9 men and 5 women with a mean age of 63 ± 8,) operated without neurophysiological monitoring with those of a group of 15 patients (10 men and 5 women with a mean age of 60 ± 5) operated with neurophysiological assessment. Two patients (one of each group) were non included in the study because the surgical procedure produced a severe cerebral haemorrhage. The patients were evaluated one week before the surgery and at 6 and 12 months follow-up according to the Core Assessment Program for Intracerebral Transplantions (CAPIT). In particular we report here the UPDRS 3° score recorded after administering a supramaximal dose of levodopa, showing the results in the medication on-stimulation on condition, considering it the best one the patient may achieve from the combined therapy. We considered also the UPDRS 4° score for dykinesia and motor fluctuations and the variation of the medical therapy calculating the levodopa equivalent dosage (LED). The comparison between pre- and post-operative motor scores and the levodopa equivalent dosage (LED) for each group of patients were performed by paired samples t-test.

Results: Neurophysiological monitoring showed a deviation from the theoretical target (calculated with CT/MRI fusion and in most patients also with ventriculography) in 34% of the cases. We did not find a different risk for cerebral symptomatic haemorrhages between the patients with or without neurophysiological monitoring

We observed a clinical improvement in both groups after 6 months from surgery but it was significant only in the monitored group. Otherwise after 12 months only the monitored patients group (just 9 of 15 patients have been checked), showed a better score than the presurgical one. We found that the DBS reduced significantly in both groups the dyskinesias and the motor fluctuations according to UPDRS 4° scores after 1 year. As regards the LED, it was relatively low after one year in all the patients, but again only in the monitored patients it was significant compared to the presurgical one.

Conclusion: Our preliminary results confirm that the intraoperatory neurophysiological monitoring is a useful tool for giving the best clinical results in the parkinsonian patients undergone DBS therapy.

P914

The efficacy of STN-DBS in advanced Parkinson's disease based on patient diaries and motor scores: One-year follow-up data

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Objective: Description of the Groningen 1-year efficacy data on STN-DBS in patients with advanced Parkinson's disease (PD) based on patient diaries and motor scores according to the CAPSIT-PD protocol.

Background: CAPSIT-PD recommends the use of patient self-reporting data (diaries) to evaluate the clinical efficacy of stereotactic surgery in PD. However, most published data on the efficacy of STN-DBS in PD are based on clinical (UPDRS)- and dyskinesia scores, without any diary data. Therefore we prospectively evaluated the use of patient diaries, as part of CAPSIT-PD, to assess the efficacy of STN-DBS in advanced PD, and correlated these data to motor scores.

Methods: 20 patients (9 M, 11 F, mean age 59 ± 7 year) with advanced PD (mean disease duration 13 ± 4 year, mean UPDRS III off-score 45 ± 14) underwent bilateral STN-DBS between 1999 and 2003. Clinical assessments were performed according to CAPSIT-PD 3 months before, and 6 and 12 months after surgery. Prior to the clinical assessments patients reported their own motor function at home, using a diary (during waking hours in 30-minute fractions, covering at least 5 consecutive days) reporting 4 clinical conditions: complete off, partial off, complete on and on with dyskinesia. Post hoc comparisons between pre- and postoperative diary data were performed, and diary outcomes were correlated to clinical motor scores (UPDRS III 'off-medication', and UPDRS III and Dyskinesia Rating Scale (DRS) 'on-medication') at 12 months after STN-DBS.

Results: At 12 months after STN-DBS the mean UPDRS III off-score (−32% from baseline, $P = 0.0001$) as well as the severity of on-dyskinesia (−57%, $P = 0.002$) improved significantly. The patient diaries showed a significant increase in on-time (+106%, $P = 0.002$), and a reciprocal reduction of both on- time with dyskinesia (−83%, $P = 0.0001$) and complete off-time (−63%, $P = 0.002$). Diary on-time was correlated with the individual percentage of reduction in UPDRS III off-score (Rho = 0.417, $P = 0.043$) and with the individual UPDRS-off and -on scores at 12 months after surgery. On-time improvement and reduction in on-time with dyskinesia on the diaries did not correlate with the reduction in the DRS.

Conclusion: STN-DBS in advanced PD improves all motor scores, and increases on-time (without dyskinesia) at 12 months after surgery based on patient diaries. In addition, patient self- reporting correlates significantly with clinically assessed (UPDRS) motor scores. Therefore, patient diaries serve as a reliable and important tool to evaluate the patient's functional, non-hospitalized status after STN-DBS and should be included in all future STN evaluation studies.

P915

Tremor induction by unilateral STN stimulation in Parkinson's disease

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Although DBS of the subthalamic nucleus is generally performed as a bilateral procedure in PD patients with refractory motor fluctuations and or dyskinesias, unilateral STN stimulation is still occasionally performed in PD patients with unilateral disabling parkinsonian rest tremor which is refractory to medical treatment. In our department we have performed unilateral STN stimulation in a total of 3 cases over the past 3 years, corresponding to 10% of our STN-DBS PD program in the same time period. These patients included 2 male and 1 female patient aged 40 years (case 1), 77 years (case 2) and 63 years (case 3) at the time of STN electrode implantation with a disease duration ranging between 5 to 10 years. Patient 3 was off any drug therapy prior to surgery for 7 months because of subjective lack of effect of 1,200 mg L-DOPA daily, while the two other patients were receiving dopaminergic therapy with an L-DOPA equivalent dose of 1,200 mg and 250 mg daily. Patient 1 responded satisfactorily regarding bradykinesia and rigidity scores but without acceptable tremor control, while patient 2 and 3 were tremor dominant with minimal degrees of bradykinesia and rigidity and dug resistant rest tremor as their chief complaint. Unilateral STN stimulation was performed according to standard procedures and resulted in exellent contralateral control of tremor in all and also to marked reduction in contralateral rigidity and bradykinesia in case 1. One to six months following STN stimualtion all 3 patients developed functionally disabling ipsilateral resting tremor. While there was a possibility of unmasking of symptoms due to postoperative complete medication wash out in case 1 there was no change in low dose dopaminergic treatment in case 2, while case 3 has remained drug free pre and postoperativly. We hypothesize that the new onset of ipsilateral resting tremor in at least two of these cases was triggered by disinhibition of a central tremor oscillator following unilateral high frequency STN stimulation.

P916

Brain perfusion SPECT before and 6 months after surgery during STN-DBS in advanced Parkinson's disease

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Objective: To assess brain perfusion changes using SPECT in advanced PD before and at least 6 months after surgery during deep brain stimulation of the subthalamic nucleus (STN-DBS).

Background: High frequency stimulation of the STN can improve motor symptoms and reduces the need for medical therapy in advanced PD. Moreover, STN-DBS can modify cerebral perfusion/metabolism even in larger cortical/subcortical areas, remotely from the site of stimulation. SPECT with the tracer ECD can provide accurate measurement of brain perfusion in PD.

Methods: 38 patients with advanced PD and medically untreatable fluctuations (age 62 ± 7; disease duration 15.2 ± 5.1 years; H&Y off-score 3.6 ± 0.7) underwent STN electrode implantation. STN-DBS was performed using stereotactic surgery with microelectrode recording and macrostimulation following MRI targeting and previously published surgical procedures. Motor function was assessed using UPDRS, AIMS, 12-hr on-off daily chart at baseline and 6 months later. SPECT was performed after i.v. injection of Tc-99m ECD (740 MBq) in PD group before and 6–7 months after surgery (DBS on). Data were compared with 22 age matched healthy controls. Statistical Parametric Mapping (SPM 99) analysis of SPET studies was performed. ANOVA was used to compare PD baseline vs. controls and PD baseline vs. 6-month follow up (repeated measures). Differences were considered significant for $P < 0.05$ corrected.

Results: At 12 months DBS-STN determined significant clinical improvement in terms of reduction of "off" medication UPDRS (−62%), daily "off" time (−28%) and dyskinesias (−37%) as well as levodopa equivalent doses (770 ± 333 to 310 ± 260).MMSE was unchanged (from 28.6 ± 0.3 to 28.4 ± 0.6). At baseline SPM analysis of ECD-SPET showed a significant hypoperfusion in the occipital gyrus of PD vs. controls. By contrast ECD-SPECT during DBS compared to baseline showed significant hypoperfusion in pre-frontal areas as well parietal region compared to baseline. No significant changes where observed in the basal ganglia and in the thalamus.

Conclusion: We found significant cortical decrements in prefrontal areas during STN-DBS compared to baseline. By contrast we did not observe reductions in subcortical areas as one would have expected if STN-DBS was acting with a "lesion-like" effect. We think these results are consistent with the view that STN-DBS increases inhibition of thalamo-cortical neurons, ultimately determining perfusion decrements in cortical projection areas.

P917

Deep brain stimulation (DBS) may be effective for dystonia: Six-month follow up

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Objective: To determine the efficacy of high frequency electrical stimulation of the GPi (Pallidal DBS) for the treatment of generalized and focal dystonia.

Background: The cause of dystonia is still unknown. The basal ganglia plays an important role in the pathophysiology of this heterogenous condition. High frequency electrical stimulation of the GPi (Pallidal DBS) has shown promise for the treatment of some movement disorders including dystonia. Recent reports suggest that pallidotomy may be beneficial for the treatment of generalized dystonia. Pallidal DBS mimics the effects of pallidotomy, therefore there is a likelihood that pallidal DBS may ameliorate the symptoms of dystonia. Some studies suggest that cervical dystonia and other focal dystonias may respond as well.

Methods: Two patients had non DYT-1 disabling generalized dystonia (ITD) and two patients had disabling cervical dystonia (CD). All patients received treatment with trihexyphenidyl, clonazepam, baclofen, tizanidine, botulinum toxin (BTX) types A and B at various combinations during the past 4 years without improvement. All patients developed clinical resistance to both BTX A and B. After discussing risks, benefits, consequences and alternatives all patients agreed to have high frequency pallidal DBS as surgical treatment. The stereotactic MRI guided surgical technique and intraneuronal cell recording were performed using standard accepted protocols. Patients were assessed using the Burke-Fahn-Marsden (BFM) Dystonia scale before and 6 months after surgery. Patient's medications were unchanged during the pre and post operative and follow-up periods. Preoperative protocol included neuropsycholological assessment, baseline brain MRI and medical clearance.

Results: Four patients (3 M, 1 F) with a mean age of 37 years (SD 3.65) were treated with pallidal DBS. Two patients (2 M) with generalized non-DYT-1 dystonia and two (1 M, 1 F) with CD. The mean BFM total score for the cohort was 25 (10–62.5) before and 16.125 (1.5–41.5) 6 months after surgery for a differential improvement of 35%. The BFM total score before and 6 months after surgery of the two ITD patients (2 M) who had bilateral pallidal DBS was 39.5 and 29 respectively for a differential improvement of 26.5%. The two CD patients who had unilateral pallidal DBS (1 M/Rt pallidal DBS; 1 F/Rt pallidal DBS) had a BFM total score of 10.5 and 3.25 before and 6 months after surgery for an improvement of 69%. No side effects nor surgical complications were observed during the immediate and 6 months post-operative period.

Conclusion: High frequency pallidal DBS appears to be a safe and promising therapeutic modality for the treatment of non-DYT-1 ITD and CD.

P918

Is advanced age a limiting factor to select Parkinson's disease patients for DBS treatment?

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Objective: To evaluate the influence of advanced age on the efficacy and frequency/type of adverse events in deep brain stimulation of the subthalamic nucleus (STN-DBS) in patients with advanced Parkinson's disease (PD).

Background: Age at surgery is considered a limiting factor for the admission of PD patients to the DBS treatment, and younger patients generally show a better improvement than older ones after surgery.

Methods: We have reviewed the clinical results of the first 32 consecutive patients operated on in our group, with a 12 months follow-up. One patient (aged 62) was excluded because of surgical side effect (intraoperative haemorrhage with good clinical recover) that could have altered the clinical outcome. Because no definite age limit is established, we have arbitrarily considered a watershed of 69 years to divide our sample between younger and older patients. Two groups were defined: younger (24 patients, mean age 56.7 $\pm$ 6.6, range 38–67) and older (7 patients, mean age 70 $\pm$ 1.2, range 69–72) patients.

Results: No significant difference was detected between the two groups as for improvement of UPDRS III, IV A and B, Qol, reduction of LEDD, neuropsychological outcome, occurrence of adverse effects. Surgical complications were scarce and not more frequent in older patients. Mild deterioration of walking and balance is present after DBS with the same frequency among the two groups.

Conclusion: Age should not be a rigid criterion to exclude older patients from this therapeutic option. On the other hand we suggest that for older patients it should be mandatory to strictly respect the other inclusion criteria: excellent general health, absence of cognitive decline (even subtle), reliable compliance and motivation, absence of walking, balance and speech deficits during on phase.

P919

Death by suicide after deep brain stimulation

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Objective: To report an unusually high rate of deaths by suicide in a large cohort of patients treated by deep brain stimulation (DBS) for various movement disorders.

Background: DBS has been established as an effective treatment for advanced Parkinson's disease (PD), essential tremor and other movement disorders. While cognitive complications of DBS have been well documented, impact on mood has not been thoroughly examined. Although suicide attempts have been occasionally described, no death by suicide has been reported so far in DBS patients, to the best of our knowledge.

Methods: Over the last 9 years, 134 patients with DBS-treated movement disorders have been followed, most of them implanted in our center. Clinical assessment included preoperative and postoperative UPDRS scores at 3- to 6-month intervals (for PD patients), an extensive battery of neuropsychological tests every year, a Hamilton HAD scale for depression and anxiety every 6 months and psychiatric interviews on demand.

Results: One patient with generalized dystonia and 4 PD patients (3.7% of the whole cohort) died by suicide over the 9-year period. Four patients had a history of depression prior to DBS, two with previous suicide attempts, two with a long-term planning of suicide, and one patient had bipolar mood swings. All but one PD patient had two DBS implantations, i.e, GPi-DBS followed by STN-DBS in 2 PD patients, STN-DBS followed by GPi-DBS in 1 PD patient, and GPi-DBS followed by VOA-DBS in the dystonia patient. Overall, multiple interventions represent 9% of our cohort. On average, suicides were committed 3.6 years after the last surgery. All patients had different DBS parameters which have been kept unchanged for several months at the time of death. All were followed by a psychiatrist on a regular basis and some were treated with antidepressant agents. Paradoxically, DBS has proved successful in all patients providing a dramatic and sustained improvement of motor function, equivalent to their best ON response.

Conclusion: Suicide may occur after DBS for movement disorders in a significant proportion of patients. The apparent prevalence of 3.7% reported in our cohort is considerably higher than both the mean rate of suicide in the normal population and an even lower suicide risk reported in the population of movement disorders patients. A previous history of severe depression accompanied by suicide attempts or suicide projects seems to constitute a risk factor. Furthermore, patients seeking multiple interventions may have an additional risk. On the other hand, this risk appears independent of either the stimulation site or electrical parameters of DBS. A careful psychiatric follow-up does not appear effective at preventing this outcome. We would therefore propose such risk factors to be actively detected before surgery in order to exclude such patients from DBS.

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P920

Double-blind multicentre study of bilateral subthalamic nucleus deep brain stimulation in Parkinson's disease: Results of the French SPARK Study Group

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Objective: To assess the effects of deep brain stimulation (DBS) of the subthalamic nucleus (STN) on motor and cognitive functions, to predict factors of outcome and safety in Parkinson's disease (PD).

Background: Deep brain stimulation of the STN is an alternative therapy for severe PD. In the largest series of patients operated on with this procedure so far, we aimed to assess the effects of surgery on motor and cognitive functions, the predictive factors of outcome and safety.

Methods: The French SPARK Group conducted a prospective multicentre study including 110 patients from four centres, 97 of whom underwent bilateral STN stimulation. Efficacy of DBS was assessed over 12 months with the Unified Parkinson's Disease Rating Scale (UPDRS), including a double-blind randomised motor evaluation. Cognition and mood were assessed with the Mattis Dementia Rating Scale, frontal lobe tests and the Beck Depression Inventory.

Results: Postoperative anatomical coordinates of the electrodes showed correct STN placement in all cases but one. In off-medication condition, the motor score improved by 57% and activities of daily living by 48%. Verbal fluency was the only cognitive test that significantly deteriorated after surgery. Mood was unchanged but decrease in motivation was observed in one quarter of patients. The mean levodopa equivalent daily dose decreased by 59%. Twenty nine patients did not receive levodopa. The preoperative on-medication UPDRS motor score was predictive of the 12-month postoperative motor score. Five patients had an intracerebral hematoma during the electrode implantation responsible for permanent after-effects in two cases.

Conclusion: Bilateral STN stimulation is an effective and relatively safe procedure for severe PD if performed in centres with expertise in targeting the STN.

P921

Low risk of major surgical complications with a minimally invasive approach with intraoperative electrophysiologic mapping in bilateral STN stimulation for Parkinson's disease

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Objective: To determine the short-term efficacy and safety of subthalamic nucleus (STN) deep brain stimulation (DBS) in patients with Parkinson's disease (PD) using a minimally invasive microelectrode recording (MER) approach.

Background: Bilateral STN DBS is an effective treatment for PD. Surgical complications may be related to prolonged operative times and a high number of MER passes during electrophysiologic localization of the target.

Methods: Quadripolar leads were implanted bilaterally under stereotactic guidance in the STN of 115 PD patients (mean age 62.4 years; 68 men, 46 women; disease duration 14.3 years). Seventeen patients had a previous pallidotomy. The target coordinates were calculated by using MRI imaging and computerized methods. Intraoperative MER was used for confirmation of the anatomical target. Only one microelectrode tract was used on each side if the STN span was greater than 3.2 mm. When the STN span was lower than 3.2 mm a second pass was made. A subset of 72 patients without previous pallidotomy was evaluated in the medication-off/stimulation-off and medication-off/stimulation-on conditions using the UPDRS subscale III, at initial programming (3 weeks post-surgery) and at 6 months post-surgery.

Results: UPDRS subscale III scores were significantly lower for the medication-off/stimulation-on condition vs. the medication-off/stimulation-off condition on initial programming (mean: 36.9%, SD: 17.4, $P < 0.001$), and at 6-month follow-up (mean: 47.8%, SD: 20.8, $P < 0.001$) in the subset of 72 patients. The levodopa-equivalent daily dose was reduced by 43% ($P < 0.001$) at 6-month follow-up. The span of the STN (by MER) was 4.8 mm (SD: 0.9, range: 3.2–7.5 mm) for the left side and 4.5 mm (SD: 0.9, range: 2.0–6.9 mm) for the right side. The average number of penetrations (MER) per implantation was 1.5 (SD: 1.0, range: 1–6) for the left side and 1.3 (SD: 0.8, range: 1–7) for the right side. No patients died of surgical complications. Eight patients died from unrelated causes. Complications included: 1 intraventricular hemorrhage (transient confusion and ophthalmoplegia); 1 asymptomatic chronic subdural hematoma (no treatment required); 2 cranial nerve palsies (mild residual unilateral sixth nerve palsy in 1; mild, transient unilateral third and seventh nerve palsies in 1); 3 infections; 1 hardware complication requiring brain lead reimplantation; 2 other hardware problems; 1 electrode placed too deep (stimulation-induced affective change requiring surgical revision). Confusion and psychiatric problems were rare and transient. Side effects from stimulation were mild and tolerable, and the majority improved with changes in stimulation parameters. Off-period symptoms, wearing-off and drug-induced dyskinesias were reduced, per patient reports.

Conclusion: Bilateral STN DBS improves the motor signs of PD. A minimally invasive technique (using the lowest possible number of brain penetrations during microelectrode recording) carries a low risk of major complications yet preserves good outcome.

P922

Back pain in patients with Parkinson's disease: A mini-invasive approach

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Objective: To monitor mini-invasive treatment in Parkinson's disease patients suffering from back pain due to partially collapsed vertebral bone.

Background: Parkinson's disease and Parkinsonisms make up a complex syndromic framework including back pain, often difficult to be diagnosed and treated. Back pain in Parkinson's disease patients may be caused by: a) uncorrect posture; b) osteoporosis, and consequently, c) vertebral body collapse. In fact, the majority of these patients are old, with compromised movements. Authors report here the results of treating Parkinson's disease patients, referring drug resistant back pain and gait disturbances resulting from partially collapsed vertebral body, with percutaneous transpedicular polymethylmethacrylate vertebroplasty (PTPV). PTPV is a therapeutic procedure, performed under neuroradiological guidance, consisting of an injection of acrylic cement as polymethylmethacrylate into vertebral body.

Methods: Six Parkinson's disease patients, 3 men and 3 women, with partially collapsed vertebral body at the X-ray control (4 cases at dorsal level, and two cases at first lumbar level), were treated with PTPV. These patients were assessed: a) with Parkinson's disease scaling UPDRS; b) with pain scale evaluation (McGill-Melzack and VAS scaling); c) with overall quality of life and sleep comfort interview; in all cases scaling was performed before and after the procedure, after 1 month and after 3 months.

The procedure was performed with patients, positioned prone, treated under local anesthesia. Polymethylmethacrylate (PMMA), mixed with liquid monomer as barium sulfate (an opacifying agent), was injected into the interstices of the vertebral body until at least 70% of the fractured bone treated was filled. After bed rest of 3 hr, while the cement cures into a hardened state, the patients were discharged home.

Results: Patients evaluated after 1 and 3 months after procedure: in all cases scaling results showed an improvement up to 60% in pain relief, 25–35% at the UPDRS scaling and up to 65–70% at the interviews on quality of life, both at first and at second interviews.

Conclusion: The correct diagnosis of drug refractory back pain in Parkinson's disease patient is underestimated. It is demonstrated that intrinsic bone innervation is responsible in determing of pain due to bone fracture. In these patients, usually, there is another pain, degenerative pain and joints diseases, due to the sensitized nociceptors in inflamed pariarticular soft tissues. Current antiflamatory compounds do not work properly. Pain relief is obtained, in case of bone fracture, injecting acrylic cement, based on the concept of narrow canal treatment. This procedure offers new possibility to improve QoL of Parkinson's disease patients, without increasing the amount of drug intake. Minimally invasive procedure of PTPV allows therapy also in old patients. At this level PTPV is easily performed, with low risk of surgical complication, under a day-hospital procedure. PTPV showed to be a safe and feasible treatment.

P923

Pallidal surgery for craniocervical dystonia (Meige's syndrome)

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Lesioning and high frequency electrical stimulation of the internal segment of the globus pallidus (GPi) has been documented to benefit patients with refractory generalized dystonia. However, little is known about the efficacy of pallidal surgery for idiopathic focal and segmental dystonia, although several small studies have suggested benefit for cervical dystonia with GPi deep brain stimulation (DBS).

In this report we describe 2 patients with intractable severe craniocervical dystonia who failed pharmacotherapy and botulinum toxin injections who were successfully treated with pallidal surgery. One patient underwent staged bilateral GPi lesioning while the other underwent simultaneous GPi DBS implantation. In both cases, sustained and significant improvement was obtained as measured by the Burke-Fahn-Marsden Dystonia Rating Scale, Abnormal Involuntary Movement Scale and Schwab & England Activities of Daily Living Scale, although time to maximal improvement was quite different.

Case 1. A 45 year-old woman whose initial symptoms began approximately 6 years earlier with bilateral facial twitching. Her condition progressed to involve involuntary contractions of eyelids, lower facial and jaw muscles, vocal cords cervical muscles and muscles of respiration. Multiple oral medication regimens failed to control her symptoms, while botulinum toxin injections provided only modest relief. She was unable to maintain employment and activities of daily living were significantly impaired. She underwent staged microelectrode guided bilateral GPi lesioning procedures with marked symptomatic improvement. Maximal improvement took place within several months. These benefits have been sustained and have persisted 5 years following the pallidotomy procedures.

Case 2. A 58 year-old man whose symptoms began approximately 3 years earlier with involuntary eyelid closure. His symptoms intensified and rapidly progressed to include involuntary jaw clenching, painful contractions of cervical muscles resulting in marked head movement, lower facial involuntary movements and significant respiratory involvement. He failed all treatment including pharmacotherapy and botulinum toxin injections. He was unable to maintain his business and required assistance for most activities of daily living. He underwent bilateral simultaneous microelectrode guided implantation of DBS leads into the GPi and although some minimal benefit was obtained after initial programming, maximal benefit occurred approximately 1 year later with significant reduction in symptoms.

These cases demonstrate the efficacy of GPi lesioning and GPi DBS for medically refractory idiopathic craniocervical dystonia in a manner similar to that shown for idiopathic generalized dystonia and spasmodic torticollis. The reversibility and flexibility of DBS provides advantages over lesioning although the time to maximal improvement and implanted hardware may be drawbacks, especially if outcomes are similar. The mechanism underlying the time differential to improvement is unclear and needs further exploration, but may be related to the more immediate disruption of upstream and downstream neural signaling with lesioning.

P924

Effect of stimulation of subthalamic nucleus on parkinsonian voice: A spectroscopic and videolaryngostroboscopic study

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Deep brain stimulation (DBS) of subthalamic nucleus (STN) has demonstrated to be safe and effective in advanced Parkinson's disease (PD), when performed in selected patients. So far, several studies and clinical evidences have demonstrated the efficacy of this treatment on motor function, but unwelcome effects have being pointed too, more and more as the number of treated patients grows. Voice abnormalities are typical features of PD and frequently, STN DBS can modify or increase voice disorders.

The aim of this study is to investigate the mechanisms that sustain voice disorders in parkinsonian patients. Voice spectroscopy and videolaryngostroboscopy were performed in 10 PD patients with hypophonia. Six of these patients were studied also after bilateral stereotaxic electrode implantation into the STN for chronic high frequency stimulation, while they were in ON-therapy and ON-stimulation state.

Both groups showed a functional disphonia. Particularly DBS-patients showed hypokinetic disphonia caused by a hypotonia of laryngeal muscles while non-DBS-patients showed a prevalence of vocal tremor and an hyperkinetic disphonia.

P925

Detrimental effects of 10 Hz STN stimulation on motor symptoms in Parkinson's disease

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A previous study described a pathological oscillatory network at 10 Hz including several motor areas in patients with idiopathic Parkinson's disease (PD,1). In the present study, we tested whether 10 Hz stimulation of the subthalamic nucleus (STN) aggravates clinical symptoms in PD patients.

Testing was performed using the UPDRS motor scale after overnight withdrawal from medication in 7 PD patients 1–3 years after bilateral implantation of stimulation electrodes in the STN. Postoperative stereotactic X-ray and superposition of electrode position on preoperative MRI-scans revealed that the position of the active electrode tip with the best clinical effect was in the upper part of the STN or the neighboring zona incerta. The patient and one neurologist were blinded to the stimulation parameters. Another neurologist gave the commands and changed the stimulation parameters. Stimulation was kept constant with respect to pulse width, pole of stimulation and stimulation voltage. Frequency of stimulation was changed randomly in the following conditions: No stimulation, 5 Hz, 10 Hz, 20 Hz, 45 Hz, 130 Hz stimulation. After a period of 10 min the rater asked the patient what he felt and started the UPDRS-scoring.

During the "no stimulation" condition patients reported consistently a familiar feeling of being in a bad condition. UPDRS-scores significantly improved in all patients with stimulation at 130 Hz proving intact stimulation devices and beneficial effects of stimulation on motor performance at the stimulation site. Stimulation at 5 Hz, 20 Hz and 45 Hz revealed no significant differences compared to "no stimulation." However, several patients reported feelings ranging from "everything fine" to "uncomfortable." Stimulation with 10 Hz evoked uncomfortable sensations in 5 out of the 7 patients. The performance in the UPDRS-motor-score was significantly worse not only compared to the stimulation with 130 Hz but also in comparison with no stimulation. Further analysis of the UPDRS-subscores revealed a significant worsening in the "akinesia"-UPDRS-score during 10 Hz stimulation compared to no stimulation. The subscores of "tremor," "rigidity" and "walking and posture" were not significantly different between 10 Hz and no stimulation.

The present study indicates the clinical relevance of pathological 10 Hz synchronization in PD that might be aggravated by 10 Hz STN-stimulation. The deterioration in akinesia could be due to involvement of higher motor areas like premotor cortex and supplementary motor cortex.

1. Timmermann et al. The cerebral oscillatory network of parkinsonian resting tremor. Brain 2003;126:199–212.

P926

A prospective, randomized trial of globus pallidus vs. subthalamic nucleus deep brain stimulation for Parkinson's disease

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Objective: We sought to compare deep brain stimulation (DBS) of the globus pallidus internus (GPi) or subthalamic nucleus (STN) in patients with advanced Parkinson's disease (PD) by conducting a prospective, randomized trial of staged bilateral DBS of either GPi or STN.

Background: Deep brain stimulation (DBS) of GPi or STN is an effective treatment for patients with disabling Parkinson's disease (PD). The therapies have not, however, been compared in a large-scale, randomized study to establish whether stimulation at one target is superior to the other.

Methods: Patients with PD with disabling motor symptoms despite optimized pharmacotherapy were randomly assigned to receive either GPi or STN DBS. DBS implantation was staged, with the first implant performed contralateral to the most affected side of the body and the second side performed >3 months later, when clinically indicated. Patients underwent neurological testing 3 or more months post-operatively after the first implantation (but before the second) in the medication- and stimulation-off (12 hr) and on states. Bilateral follow-up occurred 1 year after the second surgery and annually thereafter and was identical to unilateral testing, except that the order of stimulation state was assigned in a randomized manner, with patient and neurologist blinded to stimulator state. Evaluation included the Unified Parkinson's Disease Rating Scale (UPDRS) and a variety of other measures.

Results: To date, 32 patients (13 GPi, 19 STN) have had second-side surgery and have at least 12 months follow-up post-bilateral DBS treatment. Baseline characteristics (mean & range) of GPi and STN patients, respectively, included Hoehn&Yahr stage 3.2 (3.0–4.0) and 3.5 (3.0–5.0); age at second-side surgery 60 (47–75) and 60 (46–80) years; and off-medication UPDRS-III score 46 (18–73) and 48 (25–90). At mean follow-up of 4.6 (3–12) months for unilateral GPi DBS and 4.9 (3–12) months for unilateral STN DBS, stimulation provided significant improvement in off-medication UPDRS-III scores compared to baseline of 28% ($P = 0.001$) and 31% ($P = 0.001$), respectively; on-medication UPDRS-III scores improved by 21% and 18%. At mean follow-up of 22.2 (12–36) months for bilateral GPi DBS and 20.8 (12–36) months for bilateral STN DBS, stimulation provided significant improvements in off-medication UPDRS-III scores compared to baseline of 39% ($P = 0.001$) and 44% ($P < 0.001$), respectively; on-medication UPDRS-III scores changed by −5% and 14%. Significant improvement in UPDRS-II and IV scores and the Schwab&England scale were seen with unilateral and bilateral GPi or STN DBS. With the exception of the dyskinesia rating scale, in which only unilateral and bilateral GPi DBS provided significant improvement, there was no significant difference in the extent of improvement provided by GPi versus STN DBS.

Conclusion: Unilateral and bilateral GPi and STN DBS provided significant improvement in off-medication motor function, UPDRS II and IV scores, and functional capacity. Only patients treated with GPi DBS received significant reduction in dyskinesia scores. This was the only statistically significant difference between the two targets.

P927

The effects of pallidotomy on motor function in MPTP-treated, L-DOPA primed common marmosets

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Objective: To evaluate the effects of unilateral pallidotomy on locomotor activity, motor disability and L-DOPA-induced dyskinesia in parkinsonian common marmosets.

Background: The major motor disturbances in Parkinson's disease are thought to be caused by the imbalance in the activity of the direct and the indirect circuitry of the striatal output pathways. Following the finding that pallidotomy can reverse both parkinsonian symptoms and L-DOPA induced dyskinesia, evidence is now emerging that motoric disturbances can be caused by irregular firing patterns of the GPi of PD patients. Pallidotomy may therefore suppress abnormal GPi neuronal firing and allow the normal pattern to surface.

Methods: The effects of pallidotomy in MPTP-treated, L-DOPA common marmosets primed to display dyskinesia were investigated with special attention to the following specific issues: (i) The optimal size and location of the lesion of the medial pallidum that improves the motor deficits and dyskinesia exhibited by L-DOPA primed, MPTP treated marmosets. (ii) The effects of unilateral pallidotomy on motor activity and motor disability with and without the administration of L-DOPA on L-DOPA primed, MPTP-treated marmosets.

Results: Response to L-DOPA varied among animals so that they were divided into two groups with lower (group 1) and higher (group 2) locomotor counts. The impact of pallidotomy on the behaviour of the two groups was examined separately. Animals in group-2 showed significantly greater intensity of chorea, which may explain the increased locomotor activity counts seen in animals of this group when treated with L-DOPA. Whereas pallidotomy has no effect on basal or L-DOPA induced increases in locomotor activity in MPTP treated, L-DOPA primed common marmoset, it significantly reduced basal motor disability in group-2 but not in group-1 animals. Motor disability was similarly reduced in both groups of animals. However, dyskinesia was reduced, although only transiently in the most dyskinetic monkeys.

Conclusion: The findings of this study suggest that pallidotomy can cause improvements in disability and L-DOPA induced dyskinesia that may be specific to the MPTP treated, L-DOPA primed common marmoset and therefore may serve as guide for further assessments of stereotactic surgery in this model.

P928

The anatomic specificity of rest tremor suppression

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Objective: To report anatomical specificity for rest tremor suppression by deep brain stimulation (DBS) within the ventral intermediate nucleus of the thalamus (VIM).

Background: 38 year old man with long history of hereditary-sensorimotor neuropathy was seen in consultation for progressive tremor in left arm for the past 8 months. The tremor was most severe with action but was also present at rest and with posture. His tone was normal except for decreased arm swing on the left side. The remainder of his neurological findings were consistent with his neuropathy. The tremor did not respond to trials of L-DOPA or clonazepam. Due to the disability from his tremor he was considered a candidate for VIM DBS.

Methods: A right VIM DBS electrode (Model 3387, Medtronic, Inc., Minneapolis, MN) was placed using both microelectrode recording and intraoperative stimulation data. Tremor suppression was demonstrated at the time of surgery, and the permanent electrode was centered over this target.

Results: One month following surgery he was seen for the initial programming of his internal pulse generator. Using a unipolar configuration with the case designated positive and contact one negative (amplitude 1.0 V: pulse width 90 μsec; frequency 185 Hz) a marked (near complete) reduction in action, postural, and rest tremor was seen without AE's. With contact 2 negative (amplitude 1.0 V: pulse width 90 μsec; frequency 185 Hz) a similar reduction in rest tremor was seen with no improvement in action or postural tremor.

Conclusion: This patient demonstrates an anatomically differential response for rest tremor and action/postural tremor within the thalamus. The location for suppression of rest tremor alone was more anterior and slightly lateral when compared to the optimal site for suppression of postural and action tremor. Further investigation of other patients with complicated tremor is needed in order to better define the anatomical and neurophysiologic response identified in this patient.

P929

A comparison of short-term and long-term effects of deep brain stimulation on quality of life in patients with Parkinson's disease

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Objective: To evaluate the short term and long term effects of deep-brain stimulation of the sub-thalamic nucleus (STN DBS) on quality of life in patients with Parkinson's disease.

Background: STN DBS has been shown to improve motor function and decrease medication requirements in patients with Parkinson's disease. There is less data supporting the benefits of STN DBS on quality of life, especially for periods follow-up over 1 year.

Methods: We report quality-of-life outcomes on a cohort of 38 patients who underwent STN DBS betwen 1999 and 2001. Patients were evaluated with the SF-36 generic quality of life instrument and the PDQ-39 disease-specific quality-of-life scale before surgery, 6 months after surgery and at a long term follow-up visit (median time from surgery to long-term follow-up: 30.2 months; range 13.4–44.7 months.). Scores on the quality of life measures before surgery were compared to short and long-term follow-up scores. Quality of life measures at 6 months were also compared to long-term quality of life.

Results: In the short-term, there were statistically significant improvements in the physical function, role physical, bodily pain and role-emotional domains of the SF-36. The greatest improvements in the SF-36 were in the physical function (18%; $P < 0.0001$) and bodily pain (16%; $P = 0.0013$) domains. There was also a substantial relative improvement in the role-phyiscal domain (from a mean score of 3.8–9.5; $P = 0.041$), but the absolute scores in this domain remained quite low. The remainder of the SF-36 domains (vitality, social function, general health and mental health) did not improve in the short term. At long-term follow-up, there was still an 11% improvement over baseline in physical function ($P = 0.0068$), a 14% improvement in bodily pain ($P = 0.023$) and a sustained relative improvement in the role-physical domain ($P = 0.014$). The remainder of the SF-36 domains remained unchanged, with the exception of the vitality domain which showed continued improvement over the long term (7% improvement at long-term follow-up compared to baseline; $P = 0.024$). Five domains of the PDQ-39 (mobility, ADL function, emotional well-being, stigma and bodily discomfort) showed at least a 20% improvement at 6 months. The social support, cognition and communication domains did not change in the short term. The most substantial improvements came in the emotional well-being (22% improvement; $P = 0.0001$) and stigma (23% improvement; $P = 0.0004$) domains. At the long-term evaluation, the improvements in the PDQ-39 domains that were manifest at 6 months were maintained. However, scores for the cognition domain (which did not improve at 6 months) declined by 11% ($P = 0.012$) between the 6 month and long-term visit. Scores on the communication domain also declined between 6 months and long term (−15%; $P = 0.0011$).

Conclusion: In this cohort of patients with advanced PD undergoing STN DBS, the quality-of-life benefits present at 6 months were generally sustained over a long-term period of observation. The PDQ-39 appears somewhat more senstive to the short and long term effects of STN DBS than the SF-36.

P930

Failed subthalamic stimulation in Parkinson's disease: Can we still interfere?

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Objective: To delineate reasons behind failed STN DBS in PD and report the effectiveness and safety of corrective management based on surgical re-intervention or adjustment of electrical stimulation programming and pharmacological approach.

Background: Subthalamic stimulation is becoming the standard surgical treatment of advanced Parkinson's disease. Some patients however fail to respond adequately to surgery. The reversibility of the stimulation effects encourages corrective measures to be taken.

Methods: We have prospectively and consecutively enrolled eight patients with primary failed STN DBS, defined as sub-optimal motor improvement or persistent functional impairment. Six of them were referred from other centers. Assessment involved a careful medical history taking, neuropsychological evaluation, MR imaging and testing of the effects of stimulation on every contact. Five patients required surgical re-intervention, 4 of them unilaterally. Patients improvement was assessed individually by comparison of pre- and post-corrective measures using UPDRS-III motor and UPDRS-IVA/B clinical complications sub scores.

Results: All patients reported functional improvement after surgical or other medical corrective measures. One patients was misdiagnosed with advanced Multiple System Atrophy and was poorly responsive to treatment. All patients improved after stereotactical surgical re-intervention (range: 5.71–29.41%) and one patient after unilateral adjustment of vertical lead level (30.77%), while the other failed to show any further improvement. Adjustment of stimulation parameters for two patients improved general motor condition by 75%. Mean levodopa equivalent daily dose further decreased by 29.86%. Dyskinesias and motor fluctuations improved by 65% and 67.6%, respectively.

Conclusion: Failure of STN stimulation to improve motor symptoms is multifactorial but often safely adjustable. A multidisciplinary approach insures accurate diagnosis, optimized surgical targeting and postoperative adjustment of stimulation and PD drugs

P931

Percutaneous radiofrequency facial nerve neurectomy, selective facial neurectomy, blepharoplasty and elevation of eyebrows for treatment of facial dyskinesias

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Objective: Presentation of the results of selective neurectomy of the orbital branches of the facial nerve, blepharoplasty and elevation of eyebrows and percutaneous radiofrequency facial nerve neurectomy for treatment of facial dyskinesias.

Background: The medical treatment of essential blepharospasm is many times unsatisfactory. As the course of the disease is unknown and the recurrence rate in long term treatment of patients with botulinum toxin is high, surgical procedures aiming for symptomatic control of the disease is sometimes necessary. Denervation of the orbicularis muscle is the best surgical method for treatment of this condition. However, complications related to the uncontrolled extension of the deafferentation of the facial muscles are common.

Methods: Twenty patients with essential blepharospasm underwent selective neurectomy of the orbital branches of the facial nerve under Gasserian ganglion block with local anesthetics. The patients were kept awake and asked to close the eyelids continuously to allow direct control of the function of facial muscles after microsection of small branches of the orbicularis muscle. The operations were discontinued when the spasms ceased. The neurectomy was then followed by elevation of the eyebrows and blepharoplasty. In 36 patients with Meige's syndrome percutaneous facial nerve neurectomy under local anesthesia was performed. After identification of the trunk of the facial nerve in the stylomastoid foramen 65°C radiofrequency lesions (lasting 10 sec) were induced and repeated until facial palsy was obtained.

Results: The results with selective neurectomy were excellent in 8, good in 10 and fair in 2 patients during a mean follow-up period of 36 months. The procedure was repeated in 4 patients. There was immediate alleviation of the facial dystonic movements in all patients with Meige's syndrome; in about 6 weeks there was paryial recovery of facial muscles function and the patients were free of recurrence during a mean follow-up time of 8.5 months. The procedure was then repeated 2 to 4 times as necessary. No complications were observed.

Conclusion: Selective neurectomy and percutaneous radiofrequency facial nerve neurectomy are safe and effective treatment options for facial dyskinesias.

P932

Anatomic locus for induction and suppression of dyskinesia in Parkinson's disease patients treated with subthalamic nucleus deep brain stimulation

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Objective: To determine the anatomic site in or near the subthalamic nucleus (STN) associated with production of or reduction in dyskinesia in patients with Parkinson's disease (PD) treated with STN deep brain stimulation (DBS).

Background: Clinical observations suggest stimulation in different regions within or adjacent to the STN may produce differing motor effects. Improvement in PD features has generally been associated with stimulation in the dorsal aspect of the STN. In some patients, however, a DBS

electrode that provides excellent control of PD symptoms can also produce severe choreoathetotic or dystonic dyskinesia. To manage these patients, reduction in dopaminergic medication and/or decrease in stimulation is required. This requires careful and often challenging titration of both PD medication and STN stimulation.

Methods: We cataloged clinical observations made in 8 patients prone to STN stimulation-induced dyskinesia during the course of routine DBS programming with medication held. At the time of evaluation, these bilateral STN DBS patients had been treated with DBS for 6–60 months. During the course of evaluating each DBS electrode sequentially, we noted the effects of stimulation on PD signs and development or eradication of dyskinesia. Correlation of these clinical findings with the anatomic site producing them was accomplished by analyzing intraoperative physiological data and identifying 3-D coordinates of the respective DBS electrodes on postoperative volumetric MRI reformatted into standard anatomic planes.

Results: Following selection of the single unipolar DBS electrode that produced greatest motoric benefit, we noted the development of contralateral dyskinesia within 5–120 min in 9 of the 16 DBS leads. The mean location of the DBS electrode for these effects was 1.6 mm below the dorsal border of STN, as determined by the intraoperative physiological map. This electrode location with respect to the mid-commissural point on postoperative MRI corresponded to the coordinates of $x = -11.9 \pm 1.5$ mm, $y = -2.1 \pm 0.3$ mm, and $z = -4.4 \pm 0.5$ mm. Dyskinesia produced by the single contact were then quickly (within seconds) and completely abolished by the addition of stimulation using the next superior DBS electrode. Dyskinesia did not return upon resuming PD medication. The mean location of this DBS electrode was 1.4 mm above the dorsal border of STN, as determined by the intraoperative physiological map. This electrode location with respect to the mid-commissural point on postoperative MRI corresponded to the coordinates of $x = -12.2 \pm 1.6$ mm, $y = -0.5 \pm 0.2$ mm, and $z = -2.0 \pm 0.6$ mm.

Conclusion: We found that stimulation in the dorsal STN produced motoric improvement but in a subset of patients, also induced dyskinesia. Dyskinesia was then counteracted with the addition of a DBS electrode located superior to the dorsal border of STN. Thus, using 2 adjacent unipolar electrodes together, patients achieved excellent motoric benefit without worsening dyskinesia. The anti-dyskinetic effect may be mediated by stimulation of white matter tracts (zona inserta, H_2, and Fields of Forrel) above the STN.

P933

Long-term effects of bilateral subthalamic nucleus and globus pallidus deep brain stimulation on gait velocity, stride length, and kinematics in patients with Parkinson's disease

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Objective: To determine the long-term effects of bilateral deep brain stimulation (DBS) of the subthalamic nucleus (STN) or globus pallidus (GPi) on gait velocity, stride length, and kinematics in patients with Parkinson's disease (PD).

Background: A variety of gait problems affect patients with PD, including decreased velocity, increased cadence, diminished stride length, and reduced joint excursions. The efficacy of medication to ameliorate disordered gait diminishes in the later stages of the disease.

Methods: Eleven patients with bilateral DBS of either STN or GPi were evaluated pre-operatively and 3–4 years post-operatively using the 3-D Motion Analysis system. Temporal-spatial characteristics and kinematics of gait were determined using Expert Vision (version 6.03) and Orthotrak (version 5.02) software programs. Measurements were made under four conditions (off and on stimulation and off and on medication). Data were analyzed using Wilcoxon Signed-Ranks Tests.

Results: Significant improvements in gait stride length ($P < 0.05$), cadence ($P < 0.02$), and knee and ankle joint excursions ($P < 0.05$) were seen between the post-operative off medication/on stimulation condition and the post-operative off medication/off stimulation condition. Four subjects who were unable to walk pre-operatively off medication were able to walk post-operatively with stimulation in the off-medication state. There was no significant difference in the improvement seen in the STN compared to the GPi DBS patients. No significant changes were seen between the on-medication states, on or off stimulation.

Conclusion: Bilateral DBS of the STN or GPi was effective in improving gait velocity, stride length, and joint excursion at 3 to 4 years post-operative follow-up. Improvements were similar for patients treated with DBS at either target.

P934

Neuropsychological functioning after staged bilateral pallidal or subthalamic nucleus deep brain stimulation for Parkinson's disease

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Objective: To evaluate neuropsychological outcome of staged unilateral deep brain stimulation (DBS) of subthalamic nucleus (STN) or globus pallidus internus (GPi) in advanced Parkinson's disease (PD), as a function of side and surgical target.

Background: Previous research has suggested that DBS for treatment of PD may result in mild decrements in verbal associative fluency and other neuropsychological functions, including executive functioning and memory. Questions remain about importance of surgical target (right vs. left, STN vs. GPi) and unilateral vs. bilateral treatment in affecting cognitive function.

Methods: We evaluated 24 patients with moderately advanced PD at baseline and after each unilateral surgery as part of a staged bilateral DBS protocol. Patients were randomized to a surgical target (13 STN, 11 GPi). Initial target was left-sided in 9 STN and 7 GPi patients. Randomization resulted in two main study groups matched on age, education, and baseline motor and cognitive ability. The test battery included WAIS-R Digit Span, Digit Symbol and Arithmetic, the Trail Making Test, Letter and Animal Naming, Boston Naming Test, Rey Auditory Verbal Learning Test, Brief Visuospatial Memory Test, and the Stroop Test. The battery of tests was repeated once at 5 (range 3–12) months following unilateral DBS surgery and a second time 15 (range 8–24) months after placement of the contralateral DBS lead.

Results: The main finding was an overall significant reduction in Animal Naming between baseline and the third assessment ($P < 0.01$). There was a trend in the direction of incremental decrements in verbal associative fluency after each of the two surgeries. However, greatest effect was noted between baseline and first follow-up assessment. Comparison of all pre-op to post-op intervals by side revealed the decrements were greatest following left DBS. There were two significant effects of surgical target. Post-op evaluation following STN surgery (but not GPi) revealed lower visuomotor processing efficiency, as assessed using the WAIS-R Digit Symbol subtest. In contrast, GPi surgery but not STN was associated with a decrement in Digit Span Backwards performance between the second and third evaluation. There were no significant changes in basic language or learning and memory scores, or on the Dementia Rating Scale.

Conclusion: A few small declines in neuropsychological functioning were observed, most of which were noted only inconsistently across surgical groups and time points. Without a non-surgical control, it is difficult to gauge to what extent some of these declines reflect normal progression of cognitive motor difficulties associated with aging and progression of Parkinson's disease over the nearly two year study period. Verbal fluency showed the greatest decline, especially over the initial follow-up interval and in association with left-lateralized DBS. Results suggest that there may be subtle differences in the effects of side and surgery target on a few information processing tasks in addition to verbal fluency.

P935

Long-term efficacy of pallidal DBS for treatment of medically refractory dystonia

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Objective: To study the long-term safety and efficacy of bilateral deep brain stimulation (DBS) of the globus pallidus pars interna (GPi) in patients with primary and secondary dystonia.

Background: Dystonia is a disabling movement disorder with limited response to pharmacological therapy. While preliminary studies of bilateral pallidal DBS have shown promising results in selected cases of primary and secondary dystonia, little data exists about the long-term safety and efficacy of this therapy.

Methods: We implanted bilateral DBS leads in the GPi of 10 patients (5 females and 5 males, age range 13–63) with medically intractable primary dystonia and three patients with secondary dystonia (2 males and 1 female, age range 10–32). Six patients with primary dystonia tested positive for the DYT1 gene defect. The three patients with secondary dystonia had a history of encephalitis (2) and ischemic encephalopathy (1) during early childhood. Intraoperative MER, fluoroscopy and MRI were used to locate final target in the GPi. All patients were videotaped and evaluated with the Burke-Fahn-Marsden Dystonia Rating Scale (BFMDRS) before and at several intervals after surgery. DBS settings were slowly and systematically increased to achieve best clinical effect. We generally used large pulse widths (210–400 μsec) and high frequency (130 Hz) stimulation. Percent changes of BFMDRS scores at several intervals after surgery were calculated. All patients were followed for at least 6 months.

Results: All patients with primary dystonia showed improvement of their BFMDRS scores (best average improvement 68.8%, range 32–97%), which was progressive over time (37.6% on average at 1 month, 50.5% at 3 months, 62.4% at 6 months, 66.3% at 1 year [7 patients], 71.2% at 2 years [6 patients]). Two DYT1-positive patients showed BFMDRS improvements of 95% and 77% at 3 years follow-up. The three patients with secondary dystonia showed an average 32.6% best improvement of their BFMDRS scores. Complications included two wire fractures and one scalp infection requiring DBS lead revision.

Conclusion: We confirm that pallidal DBS is a safe and effective therapy in selected patients with medically intractable dystonia. Patients with primary dystonia consistently showed better results than those with secondary forms of dystonia. Clinical improvement was progressive and most evident 6–12 months after surgery. Long-term follow-up at 2 and 3 years showed maintained improvement of BFMDRS scores.

P936

Improvement of post-ischemic hemidystonia with low-frequency subthalamic deep brain stimulation

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Objective: To study the safety and efficacy of subthalamic deep brain stimulation (DBS) in a patient with post-ischemic hemidystonia.

Background: DBS is rapidly emerging as an effective treatment for medically refractory dystonia. While the globus pallidus pars interna (GPi) is most frequently targeted, clinical improvement of dystonia has been described also after subthalamic DBS.

Case Report: A 24-year-old female developed left hemidystonia 9 months after an ischemic infarct of the right basal ganglia at age 6. Symptoms progressively included spasmodic contractions of the left upper and lower facial muscles, involuntary left hand clenching, painful abduction and elevation of the left arm above the shoulder, left leg extension at the knee, foot inversion and toe curling. Dystonic contractions caused severe disability secondary to inability to use the left arm and hand and severe difficulty walking. She tried numerous medications without clinical benefit, including baclofen, carbamazepine, clonazepam, topiramate, levodopa, trihexyphenidyl, amitriptyline, diazepam, gabapentin, pramipexole, paroxetine and fluoxetine. Due to extensive damage of the right pallidum, we opted to implant a DBS electrode in the right subthalamic nucleus.

Methods: A unilateral DBS electrode (Medtronic model 3387) was implanted using MRI, microelectrode recordings and macrostimulation. The deepest contact (0) was positioned at the physiologically defined base of the right subthalamic nucleus. Final electrode position was confirmed using intraoperative fluoroscopy and post-operative MRI. The Burke-Fahn-Marsden Dystonia Rating Scale (BFMDRS) was used to evaluate the patient's functional status at baseline and one and three months after surgery.

Results: BFMDRS scores improved from 39.5 at baseline to 21.5 (45.6%) 1 month and 18 (54.5%) 3 months after the initiation of subthalamic stimulation. High frequency stimulation (130–185 Hz) was clinically ineffective. The best clinical results were observed with stimulation at lower frequency (50–60 Hz) and large pulse width (400–450 msec). The most dorsal contact (3) was consistently the most beneficial. Different from what is observed with pallidal stimulation, dystonia may improve rapidly after programming at the most effective settings.

Conclusion: Subthalamic DBS was effective in a patient with medically refractory secondary hemidystonia. Contrary to what is observed in Parkinson's disease, low frequency stimulation and a large pulse width yielded the best results. Rapid clinical improvement was observed at the most effective stimulation settings.

P937

Parkinson's disease surgery clinical outcomes and complications, one-year follow-up: Venezuelan experience

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Background: Parkinson's Disease (PD) surgery Deep Brain Stimulation type (DBS) it's a worldwide accepted surgical procedure to improve the clinical complication attributable to the chronic use of levodopa. Side effects associated to this surgery have been pointed out for some movement disorders groups around the world. We want to describe the clinical outcomes, side effects and limitations of PD surgery DBS type in Venezuela.

Methods: We included in this protocol to six (6) consecutives, PD patients aged from 52 years old to 72 years old, four (4) males and two (2) females, mean age disease onset of nine (9) years, H-Y scale III (5 patients) and IV (1 patient) with motor fluctuations and dyskinesias refractory to all possible medical strategies. Patients underwent to bilateral Sub-thalamic DBS using a tetrapolar electrode (Medtronic Co., MN) connected to a bilateral Stimulator Soletra model (Medtronic Co., MN). The targeting was realised with a cranial CT previous stereotactic frame placement in the skull (CRW Radionic Co., USA). Single units Microregistering was used to determine the neurophysiological characteristics of subthalamic nuclia. We use as assessment parameters the UPDRS scale (part III) and the Activity of daily living scale PDQ39 at baseline and 6, and 12 months after surgery.

Results: At 6 months evaluation patients showed and average of improvement of 68.8% in the UPDRS part IIII and 38.6% in the PDQ30 scale. The levodopa dose was decrease in 65% and all the patients but one could stop other ant-parkinsonian medication. Voice and gait improved showed an average of improvement of 15% and 25% in the respective scale post surgery. At 1 year evaluation patients showed an average of improvement of 65% in the UPDRS part III, the average of improvement in the PDQ39 scale was 38%. Voice and gait outcomes showed no changes Depression was a common finding in all the patients ($n = 6$), chronic infection was observed in one patient and a laryngeal stridor for capsular stimulation was reported too.

Conclusion: Our PD patients showed at one year follow up an average of improvement of 65% in the UPDRS part III and 38% in the activities of daily living (PDQ39). Depression and infection and capsular iatrogenic effects were reported too. Probable the poor improvement in the activities of daily living could be related to the depressive syndrome observed.

P938

The influence of subthalamic deep brain stimulation on psychological and somatic symptoms and distress in patients with Parkinson's disease

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Objective: To evaluate the effects of bilateral subthalamic deep brain stimulation (STN-DBS) on psychological symptoms and distress 3 weeks, 9 weeks, 3, 6 and 12 months after surgery in patients with Parkinson's disease (PD).

Background: STN-DBS is an effective treatment to improve motor function in patients with advanced PD. The effects of STN-DBS on mood are not clear. Some studies reported positive changes in mood, others an

adverse influence. Therefore we have performed a prospective study to examine the effects of STN-DBS on mood and quality of life.

Methods: The assessment of distress used in this study was the Symptom Checklist-90-R (SCL-90-R), which is a self-report questionnaire that measures how much patients were affected by non-specific somatic and psychological symptoms. The assessment was carried out on 33 PD patients before STN-DBS (6 weeks (t_1) and 2 weeks (t_2) = baseline data (t_b)) and 3 weeks (t_3), 9 weeks (t_4), 3 months (t_5), 6 months (t_6), 12 months (t_7) after chronic bilateral deep brain stimulation of the STN.

Results: An analysis of variance for repeated measures was performed using six assessment times (a = 0.05, two-sided). The symptoms scales indicated following results: Somatization (F = 18.003, $P = 0.000$), Interpersonal Sensitivity (F = 6.434, $P = 0.017$) and Anxiety (F = 12.404, $P = 0.001$): The scores improved significantly after surgery and were stable over one year. Following scales indicated no significant change, but a trend toward improvement from baseline to the other time scores: Obsessive-Compulsive (F = 4.014, $P = 0.055$), Depression (F = 3.343, $P = 0.078$) Paranoid Ideation (F = 4.089, $P = 0.053$) und Psychoticism (F = 3.328, $P = 0.079$). The scales Phobic Anxiety (F = 2.023, $P = 0.166$), Hostility (F = 2.844, $P = 0.103$) and the Positive Symptom Distress Index (F = 2.496, $P = 0.125$) show no significant change after surgery. The Global Severity Index (F = 8.221, $P = 0.008$) and the Positive Symptom Total (F = 12.189, $P = 0.002$) show a stable improvement after surgery.

Conclusion: This report on the effects of STN-DBS on mood and quality of life shows an improvement of the severity in some of the psychological and somatic symptoms and a significant reduction of distress. Our results suggest that the STN-DBS reduces the burden of psychological and somatic symptoms and distress in patients with PD.

P939

The 2003 "census" of the Italian Group on Deep Brain Stimulation: Questionnaire results

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Objective: We present the questionnaire results of the Italian Group on DBS in order to have a census on DBS activity in Italy.

Background: Twenty-two different Italian Centers, expert on deep brain stimulation (DBS) surgery or follow-up, participated at the study and a "census" has been completed by September 30th, 2003.

Methods: A brief questionnaire of 21 different items was sent to all the neurologists and neurosurgeons involved in the DBS. All the questions had a deadline at June 30, 2003. 23 Centers completed the census, but 2 of these didn't start DBS activity before the deadline, so they were excluded from the statistical analysis.

Results: At June 30 2003, 608 Italian subjects underwent to DBS in Italy: 527 for Parkinson disease (PD), 30 for Essential tremor (ET), 30 for dystonia and 21 for other diseases (headache, tremor in MS, etc.). The DBS management activity involved at "full-time" (mean): 2.15 neurologists and 1.77 neurosurgeons per center. The patient screening was done by the neurologist in 100% and by the neurosurgeon and neurologist in 10%. 58% used MRI-CT fusion technique or IOM to localize the final target. The major complications of DBS surgery were: symptomatic bleeding (1.9%), asymptomatic bleeding (1.9%), and infections (3.5%). The neurologist alone did the chronic DBS follow-up in all the centers.

Conclusion: In Italy, a large number of patients underwent to DBS surgery with minor complications in comparison to the literature data.

P940

Deep brain stimulation (DBS) treatment for dystonia: A neurophysiological intraoperative monitoring study

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Objective: We report the electrophysiological intraoperative monitoring (IOM) of GPi of eight dystonic subjects that underwent to micro-recording and micro-stimulation for the definitive macroelectrode positioning in the ventro-postero-lateral part of GPi.

Background: pallidal deep brain stimulation (DBS) of GPi is a promising treatment option for medically intractable dystonia even if the pathophysiological mechanism of dystonia is still debate and controversial neurophysiological features are reported from microelectrode recordings in humans.

Methods: Eight subjects with primary dystonia were studied: a patient with generalized DYT-1 positive dystonia, four patients with multisegmental DYT-1 negative dystonia, one with generalized DYT-1 negative dystonia and two with secondary hypossic dystonia. In all the subjects except one, all the oral medicaments were withdrawal before and during surgery. The GPi IOM were performed without any anaesthesia by using a FHC-microelectrode (1 Mohm) and by recording with an Axon Instrument Device, in order to evaluate the GPi neuronal activity pattern and the adverse effects secondary to microstimulation on the optic tract and internal capsule.

Results: Compared to the reports of other Authors, we find the typical slow mean discharge rate and the typical burst-pause pattern in GPi neurons only in the two subjects with secondary dystonia. In the subjects with primary dystonia we observed a sustained tonic high frequency firing rate, except in the patient who assumed oral baclofen. The IOM of GPi was useful to localize the final target in all the subjects.

Conclusion: we believe that IOM of GPi during DBS surgery for dystonia is a useful technique to localize the definitive electrodes position. Moreover, the IOM is also important to better understand the pattern of neuron discharge in dystonia when any drugs are taken off.

P941

Suicide risk in patients with Parkinson's disease undergoing subthalamic stimulation

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Objective: To determine the frequency of completed and attempted suicides following subthalamic deep brain stimulation (STN DBS) in patients with advanced Parkinson's disease (PD) and to describe five of these patients.

Background: Psychiatric symptoms following life-altering surgical procedures in general have been documented. A variety of psychiatric symptoms have been reported to follow STN DBS for PD. The causes of psychiatric symptoms following STN DBS in PD can be separated into four analytical categories: preoperative psychiatric vulnerabilities and conventional psychiatric risk factors; operative and DBS-related factors involving the STN limbic region and surrounding fibre tracts; dopaminergic medication withdrawal and associated psychiatric symptoms; and psychosocial factors including psychological adjustment in response to significant motor and functional changes, or the loss of the "sick role" of the patient and family. The baseline rate of completed suicides in PD is 10-fold lower than the general population (one year incidence of 0.016% compared to 0.16% respectively).

Methods: Sixteen centers were surveyed worldwide for the total number of STN DBS PD patients operated within their centers, the number of completed and attempted suicides and the duration between surgery and the attempt. Descriptive case reports were requested to identify underlying contributory factors. The literature was reviewed to identify further cases.

Results: A 50% response rate was obtained from the survey with a total of 406 STN DBS patients. There were two (0.5%, 3 months and 3 years after surgery) completed suicides and seven (1.7%, average 11.4 months after surgery) suicide attempts. Three patients attempted within the first two post-operative months and four patients attempted between 6 to 24 months after surgery. The literature revealed an additional two completed suicides from 73 STN DBS patients (2.7%) (1,2) from centers not included within this survey and an additional four of 80 patients (5.0%) attempting suicide between 3 months and 5 years after surgery. Four patients with attempted suicides and one with a completed suicide are reported in greater detail. The patients with attempted suicides utilized means associated with high risk.

Conclusion: In contrast to the underlying low suicide risk in the general PD population, our survey results suggest an elevated risk in the patients

with advanced PD undergoing STN DBS. The case reports suggest a multifactorial etiology. Valid predictive factors, including pre-morbid risk, have not yet been determined. Suicide represents perhaps the most serious, yet potentially modifiable, post-operative risk. The seriousness of this adverse effect warrants that the identification of predictive factors and institution of preventative measures should be a part of the PD surgical program.

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P942

Side effects of subthalamic deep brain stimulation for Parkinson's disease

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The efficacy of subthalamic deep brain stimulation in severe Parkinson's disease with motor fluctuations is well documented. However, various side-effects related to this procedure can be observed and are not always properly documented. Besides technical and peri-operative complications, several psychiatric, neuropsychological and orthopaedic problems can occur after DBS. We compared the prevalence of such complications in 20 PD patients having undergone bilateral subthalamic DBS and 20 fluctuating PD patients under drug therapy only, followed during one year. Both groups were matched for age, disease duration, "off" UPDRS motor scores and MMSE scores. The following parameters were analyzed: percentage of day "off", mean UPDRS ADL scores (on medication, on DBS), best "on" UPDRS motor scores, duration and severity of dyskinesias, prevalence of falls, fractures, psychiatric events, orthopaedic surgery, number of unscheduled visits and days of hospitalization (excluding DBS), and self-reported adverse reactions.

Mean age was 64 $\pm$ 8 in the DBS group and 66 $\pm$ 7 in the drug-treated group. Disease duration was 13.5 $\pm$ 4 years vs. 12.4 $\pm$ 3.9 years. "Off" UPDRS motor scores were 42.5 $\pm$ 8 vs. 44 $\pm$ 9.5. Mean percentage of day "off" was 9.5 $\pm$ 5.4 vs. 33.6 $\pm$ 8.5 ($P < 0.001$, unpaired t). Mean UPDRS ADL scores were 22.2 $\pm$ 6.4 vs. 36.1 $\pm$ 8.3 ($P < 0.001$). Mean levodopa + levodopa-equivalents (dopamine agonists) daily doses were 823 $\pm$ 134 mg vs. 1,753 $\pm$ 532 mg ($P < 0.0001$). UPDRS dyskinesia scores were 2.9 $\pm$ 1.5 vs. 5.9 $\pm$ 2.1 ($P < 0.001$). Among the DBS group, 11/20 patients experienced frequent falls, mostly within 3 months from surgery. Falls caused fractures in 6 cases. Falls were reported by 9/20 patients in the drug-treated group but only 1 had a fracture ($P < 0.03$ Mann-Whitney). In the DBS group, 4 patients required hip (2) or knee replacement (2) during the 1-year follow-up. Psychotic episodes or acute confusional states were reported in 5 patients of the DBS group (4/5 in the first 3 months) and 7 patients in the drug-treated group. Memory problems were reported by 9/20 DBS patients vs. 10/20 in the drug-treated group. Number of days of hospitalization were 9.4 $\pm$ 8.6 vs. 4.2 $\pm$ 3.4 ($P < 0.02$, unpaired t). Number of unscheduled visits were 2.8 $\pm$ 1.3 vs. 1.2 $\pm$ 1.3 ($P < 0.001$). We conclude that DBS improved overall quality of life but caused significantly more serious falls, orthopaedic complications and unscheduled visits or hospitalizations. Psychiatric events or self-reported memory problems were not significantly different between DBS and drug-treated patients.

P943

Deep brain stimulation (DBS) of the subthalamic nucleus (STN) and thalamic ischemia: A report of two cases

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Objective: To report the occurrence of thalamic ischemia associated with impaired verbal fluency in two patients undergoing subthalamic deep brain stimulation for the treatment of Parkinson's disease (PD).

Background: Deep brain stimulation of the subthalamic nucleus represents a significant advance in the treatment of advanced Parkinson's disease. Neuropsychiatric complications after surgery are not unusual, however, and may affect both behavioral and cognitive domains. Etiologic factors may include electrode passage or placement, field effects, anesthetic effects, progression of PD, dopaminergic medications, and worsening of pre-morbid psychopathology. The author now reports a previously unrecognized cause of post-operative neuropsychiatric impairment.

Case Reports: Patient 1 was a 67-year-old male who first developed symptoms of PD at age 48. He began treatment with levodopa at age 49, and by age 55 had developed motor fluctuations with dyskinesia. By age 67, he was having severe motor fluctuations on levodopa 1,650 mg/day, pramipexole 3.75 mg/day, and amantadine 200 mg/day. Cognitive function was intact. The patient underwent left STN quadripolar electrode placement uneventfully. Post-operatively, he was noted to have an expressive language disturbance. MRI with diffusion-weighted magnetic resonance imaging (DWI) revealed a 1 $\times$ 2 cm acute ischemic lesion in the superolateral aspect of the left thalamus and adjacent white matter, as well as chronic cerebral white matter disease. At 6 weeks, repeat MRI showed resolution of the thalamic lesion. At 8 weeks, subjective language impairment had gradually improved to 90% of baseline.

Patient 2 was a 70-year-old male who first developed symptoms of PD at age 59. He began dopamine agonist monotherapy at age 62 and added levodopa at age 68. At age 69, he began to have severe orthostatic hypotension. By age 70, he was having severe PD symptoms despite optimized medical therapy consisting of levodopa 300 mg/day, ropinerole 1.5 mg/day, fludrocortisone 0.2 mg, and midodrine 15 mg/day. Cognitive function was intact aside from mild frontal dysfunction. The patient underwent left STN quadripolar electrode placement uneventfully. Post-operatively he was found to have a language deficit consisting of impaired semantic and phonemic fluency with sparing of comprehension and repetition. MRI with DWI revealed an acute 7 $\times$ 11 mm infarct involving the left thalamus.

Conclusion: The location and timing of each ischemic lesion suggests a causal relationship between subthalamic electrode implantation and thalamic ischemia. Possible mechanisms include edema adjacent to small penetrating arteries (with resultant vascular compression), vasospasm of small penetrating or choroidal arteries, or an as yet unknown effect of electrical stimulation on small blood vessels. These cases may shed additional light on our understanding of neuropsychiatric complications in deep brain stimulation of the subthalamic nucleus.

P944

DBS electrode electric field potentials: Calculated solutions and implications

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Objective: The biophysics of deep brain stimulation (DBS) remains unclear. We have been pursuing an intensive investigation into the mechanisms of DBS by first attempting to solve the electric field equations for 1 cylindrical contact, and then for all four contacts in all of their possible monopolar and bipolar configurations (based on the Medtronic model 3387-40 electrode). Although solutions for infinite wires and point source fields are readily available, a finite cylindrical contact presents challenges, particularly in its boundary conditions.

Methods: We arrived at a unique solution for solving the charge density distribution on the electrode contact. From this, based on a discrete electric charge method, we were able to solve for a representation of the electric potential around a single contact. Using a geometric expansion, the electrical field potentials for 4 finite cylindrical ring contacts and their interactions were also solved.

Results: Distribution of the potentials are derived and shown for all four contacts. The 75% and 10% 'shells' of the voltage falloff are shown in transparent relief in each figure. We also found that, based on our derivations of the distribution of field potentials, the potential can drop to still 1/10th of its value well over 10mm from the electrode surface.

Conclusion: These results suggest that a typical 4-contact STN DBS electrode may have notable effects even in a homogeneous tissue environ-

ment well outside of the STN itself, even with optimal placement. Our solutions also allow us to use a more accurate DBS model in our computational studies of basal ganglia circuitry. Knowledge of the potential created around these electrodes may have signficant implications for how these stimulators are employed and programmed.

P945

Ex-vivo gene therapy with modified retinal pigment epithelial cells without attachment to microcarriers for parkinsonism

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Objective: To test the feasibility of human retinal pigment cell (hRPEC) mediated ex-vivo gene therapy without attachment to microcarriers in PD.

Background: hRPEC form the blood retinal barrier, have specialized local immunosuppresive properties and secrete small amaounts of dopa. We have previously shown that intrastriatal transplantation of hRPEC attached to microcarriers ameliorate parkinsonism in PD patients and in animal models of PD. However, microcarrier attachment involves introduction of a foreign body into the brain and increase the likelyhood of a host immune reaction. We tested the ability of hRPEC to form spontaneous spheres or "balls" which can then be transplanted into the brain.

Methods: We transplanted epithelial "balls" of hRPEC-GFP (green florescent protein) into the striatum and nigra of seven, 6-OHDA lesioned hemiparkinsonian (HP) Sprague Dawley rats. A recombinant lentivirus (rLV) was used to transfect the hRPEC grown in culture. Rats received a unilateral stereotaxic injection of 6-OHDA to cause HP state. hRPEC-GFP were grown on fibrinogen coated dishes. One the day of transplantation, the monolayer was scraped and allowed to form spontaneous "balls" by partial mechanical scrapping of the dish and leaving the scrapped monolayer in the dish for an additional 2 hr. These epithelial "balls" were then washed out into HBSS and gently pipetted to get a uniform suspension and transplanted into the striatum and the nigra of the rats. Animals were allowed to survive after surgery for 1, 2, 3 or 4 weeks. After euthanasia, the brain was perfused with fixative, harvested, croprotected and sectioned into peices. Coronal brain sections were made and observed for hRPEC expressing GFP under a fluorescent microscope. Adjacent sections were stained with cresyl violet to observe the cell morphology and the graft location. The sections with transplants were stained for tyrosine hydroxylase (TH), dopa decarboxylase (DDC), vesicular monoamine transporter (VMAT-2) and the RPE specific marker, EMMPRIN.

Results: There was no teratogenesis, tumorogenesis or morphological transformation of hRPEC-GFP even after 62 weeks in tissue culture dish. We could target the cells successfully to striatum and nigra and the graft was fluorescing with GFP and could be stained for DDC, EMMPRIN and VMAT. There was no host immune reaction observed at the graft locations. The grafts survived without immunosuppression. There was no host derived TH cell sprouting towards the graft.

Conclusion: We show here that hRPEC can survive xenotransplantation without attachment to microcarriers and without immunosuppression if they are allowed to form spontaneous balls. Our results suggest that ex-vivo gene therapy for PD using genetically engineered hRPEC without attachment to microcarriers is feasible and stable without the need for immunosuppression for up to 4 weeks. This modality of treatment shows considerable promise to alleviate symptoms in PD.

P946

Ipsilateral hyperhidrosis as a side effect of subthalamic deep brain stimulation

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Objective: To describe an unusual side effect of subthalamic deep brain stimulation (STN DBS).

Background: STN DBS is an effective treatment for medically intractable Parkinson's disease. Besides the subthalamic nucleus itself, a variety of structures within the subthalamic area can be affected by DBS, potentially causing unwanted side effects. Although hyperhidrosis has been mentioned anecdotally as a possible side effect of STN DBS, little evidence has been presented concerning this phenomenon.

Case Report: A 52 year-old man with a 17-year history of Parkinson's disease was implanted with bilateral subthalamic DBS leads to treat severe levodopa-induced motor fluctuations. He showed a positive and sustained response to STN-DBS, with a 47.1% improvement in UPDRS II and III as compared to his preoperative scores. During an analysis of the effectiveness of various stimulation parameters, we observed unexpected hyperhydrosis during high energy stimulation at contact 1. This phenomenon was not evident using similar energies of stimulation at contacts 0, 2, or 3 and was consistent both on- and off-medication, suggesting a specific effect of electrical stimulation. During unilateral stimulation, the patient would only perspire on the half of the body ipsilateral to the implanted electrode. Hyperidrosis occurred within one minute of programming and subsided 5 to 10 min following stimulation cessation.

Conclusion: We report a rare and reproducible side effect of STN DBS. The stimulation field generated by DBS in the subthalamic area encompasses many different structures. Given the proximity of the hypothalamus to the STN, it is possible that the field generated using high energies of stimulation at contact 1 of the DBS electrode affected the hypothalamus, an essential structure in controlling body hidrosis. Ipsilateral hyperhidrosis is a rare phenomenon that clinicians and programmers may encounter when administering DBS therapy.

P947

Predicting success after deep brain stimulation placement in the subthalamic nucleus in Parkinson's disease patients

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Objective: To evaluate what factors from patient demographics, preoperative studies, intraoperative characteristics or postoperative programming correlated with symptomatic improvement after Deep Brain Stimulation (DBS) in the subthalamic nucleus (STN) of patients with Parkinson's disease (PD) using a global improvement scale.

Background: From July of 1997 to December 2000, we placed DBS electrodes in the STN of 47 PD patients at Emory University School of Medicine. Three of these patients did not have idiopathic Parkinson's disease. None of these patients improved and were excluded from the final analysis. One patient was lost to follow-up. Of the 43 remaining patients the mean follow-up was 28.6 $\pm$ 13.2 months (range 3 months to 57 months). The average age of the patients was 57 $\pm$ 10 years and duration of disease 13.6 $\pm$ 6 years. Twenty-two (51%) patients were male and 38 (88%) right-handed. Thirteen (30%) had prior pallidotomy or thalamotomy.

Results: Analysis of demographics demonstrated that younger patients did better (Spearman rank correlation $r = -0.42$, $P = 0.0029$) while sex and handedness did not significantly correlate with improvement. A normal preoperative MRI correlated with better outcome (Wilcoxon rank-sum test, $P = 0.0005$) and third ventricle size negatively correlated with improved outcome ($r = -0.29$, $P < 0.0001$). A previous thalamotomy or pallidotomy on the opposite side or same side did not correlate with outcome. Intraoperatively, the number of microelectrode tracks needed to complete the mapping procedure was negatively correlated ($r = -0.29$, $P = 0.043$) with better outcome and the presence of a "minilesion" effect (Wilcoxon rank sum test, $P = 0.023$) correlated with better outcome. The number of kinesthetic cells, map fit and other electrophysiological characteristics did not appear to correlate with outcome. Finally, the initial DBS voltage setting required for symptomatic control ($r = -0.35$, $P = 0.021$) and the voltage at 1 year ($r = -0.35$, $P = 0.030$) correlated negatively with better outcomes.

Conclusion: Despite our finding that increasing age, abnormalities on preoperative MR imaging and the increased width of the third ventricle were negatively correlated with outcome, improvement in clinical symptoms still frequently occurred. While we do not believe these patients should be excluded from surgery, these observations suggest that more modest outcomes may be anticipated.

P948

Assessing subjective improvement and disability in patients with dystonia of the neck in generalized dystonic syndromes treated with botulinum toxin followed by deep brain stimulation

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Objective: To compare subjective improvement and disability scores in patients that have undergone botulinum toxin A injections for dystonia of the neck in generalized dystonic syndromes with deep brain stimulation (DBS) done subsequently in the same patients.

Background: Dystonia of the neck is a significant cause of discomfort and disability. It has been shown that botulinum toxin can be of benefit for cervical dystonia. Recently, DBS has been used to treat dystonia, though this is usually in the setting of a more generalized phenomenology. Within the spectrum of generalized syndromes, data on the effectiveness of botulinum toxin given for the treatment of dystonia of the neck as compared to DBS is limited. The goal of this study is to look at both subjective improvement and disability scores in patients with generalized syndromes given botulinum toxin for the cervical component of their condition. We then compare this to similar measures in the same patients who went on to have DBS therapy.

Methods: A retrospective review of handwritten and electronic medical records was conducted.

Results: At our institution, two patients had undergone botulinum toxin type A injections for dystonia of the neck followed by DBS. Patient 1 is a 51-year-old man with a 44-year history of generalized idiopathic torsion dystonia. Prior to botulinum toxin therapy, his dystonia of the neck was characterized by left torticollis, right laterocollis, with mild to moderate hypertrophy of the right sternocleidomastoid, left splenius capitus, and right lateral scalene muscles. His disability was 4 (severe and disabling). After botulinum toxin injections, at best he reported 90% subjective improvement over baseline with no change in his disability score. Prior to DBS, his Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) disability score was 13. After unilateral DBS of the left globus palludus interna, this improved to 8. Patient 2 is a 67-year-old woman with generalized dystonic tremor and dystonia of the neck. Prior to botulinum toxin therapy, her dystonia of the neck was characterized by retrocollis with a disability of 3 (moderate spasm with moderate functional impairment). With botulinum toxin injections she reported a 100% subjective improvement over baseline with a disability of 2–3 (moderate spasm with minimal/moderate functional impairment). Prior to DBS, her TWSTRS disability score was 7. After unilateral DBS of the left ventral intermediate thalamic nucleus, this improved to 1.

Conclusion: In both patients with generalized dystonic syndromes, the use of botulinum toxin injections for dystonic neck posturing did provide near complete (90% or greater) subjective improvement, with minor if any reduction in overall disability. These patients then experienced significant reduction in disability after undergoing unilateral DBS to treat their generalized syndrome. These case reports suggest that botulinum toxin effectively treats the symptoms of neck dystonia, a significant component of generalized syndromes. However, other features of the syndrome contribute greatly to overall disability, which can be reduced with DBS.

P949

Diffuse Lewy body disease with late onset of parkinsonian syndrome

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Objective: To compare the interval time for the onset of neurological signs in Lewy body disease (LBD) cases, diagnosed as POSSIBLE by neuropsychological Imaging and ElectroEncefaloGraphic (EEG) examination.

Background: The LBD is a dementia syndrome characterized by precocious neuropsiychological signs as cognitive decay, visual allucinations and fluctuacting disorders of awareness.The fluorodeoxyglucose positron emission tomography (FDG PET) seems to have a limitate value in differential diagnosis to Alzheimer Disease; moreover a relatively distinct EEG frequency pattern has been correlated to fluctuacting awareness disturb. After several years (at least two) can show oneself a Parkinsonian Syndrome.

Methods: We follow up three cases, two males aged 63 and 67 years and a female aged 66 years on the onset of dementia, defined as LBD POSSIBLE by clinical, neuropsychological, Imaging and EEG assesment, as regards to clinical progression and particularly to overlapping of an Extrapyramidal Syndrome to cognitive and mental disorders.

Results: The mean age, at the onset of dementia, was 65.3 years. After 4, 6 and 10 years respectively, appeared a Parkinsonian Syndrome, bilateral and axial, whose main signs were tremor, bradykinesia, rigidity and postural imbalance. The efficacy of Levodopa treatment (250–500 mg plus carbidopa 25–50 mg) has been moderate, but implicated an additional neuroleptic therapy (clozapine), besides the basic dosage.

Conclusion: The time span between the onset of dementia and the appearance of Parkinsonian Syndrome is widely variable in LBD. The neuropsychological assesment is precious and fundamental for orientating to follow up the extrapyramidal syndrome, incoming after several years also.