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MOVEMENT DISORDERS I

ORAL PRESENTATIONS

1/OR01

DEEP BRAIN STIMULATION BEFORE THE INTRODUCTION OF DBS

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Objective: Deep brain stimulation (DBS) is an established treatment for movement disorders. It is generally acknowledged that the development of DBS as we know it today started with the publication of Benabid, Pollak, et al in 1987 on thalamic DBS for tremor. This technique gained momentum in the mid-Nineties after the introduction of STN DBS. The aim of this presentation is to review the gestational era of DBS before 1987.

Methods: The literature was reviewed concerning DBS before 1987.

Results: The origin of DBS can be traced back to the practice of intra-operative electrical stimulation, used for target exploration prior to lesioning, during the early years of stereotactic functional neurosurgery. During the 60s, Sem-Jacobsen and others implanted externalised electrodes which were used for intermittent stimulation and evaluation during weeks or months. In the early 70s Bechtereva treated PD patients using "therapeutic electrical stimulation" through electrodes implanted for up to 1.5 years. In the 70s and early 80s the term Deep Brain Stimulation was coined and few groups attempted treatment of Parkinson's disease, non-Parkinsonian tremor and dystonia with high-frequency stimulation using chronically implanted DBS systems. Un-sophisticated hardware, together with the general decline of all surgery for PD following the introduction of levodopa, may have contributed to the lack of popularity of old-times DBS.

Conclusion: Deep brain stimulation has a long but often unnoticed history before 1987. It is to the credit of the Grenoble Group to have reinvented, modernised and expanded modern DBS in surgical treatment of movement disorders.

2/OR02

PPN DBS SURGERY FOR GAIT DISORDERS IN PARKINSON'S DISEASE

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3/OR03

RELATIONSHIPS BETWEEN GAIT DISORDER AND FOREL'S FIELD DURING CHRONIC SUBTHALAMIC STIMULATION FOR SEVERE PARKINSON'S DISEASE.

Key-words: Deep Brain Stimulation, Parkinson's disease, Gait Disorder, Forel's Field.

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Objectives: Chronic stimulation within the subthalamic region dramatically alleviates long term motor complications of severe Parkinson's disease. Gait disorder is still one of the most challenging symptoms because it is still poorly improved and its appearance during chronic stimulation limits the control of motor improvement. We hypothesized that stimulation-induced (SI) gait disorder could be related to modulation of structures involved in forebrain - basal ganglia - tegmentum circuitry implicated in locomotion.

Methods: One hundred contacts used for chronic stimulation were located in reference to the subthalamic nucleus (STN) in 50 consecutive parkinsonians implanted bilaterally. For each patient, coverage of subthalamic structures, STN, zona incerta, Forel's fields (FF), by the contacts was determined using co-registration of preoperative anatomic MRI and postoperative CT-scan and reconstruction of slices along electrodes. Walking falls, freezing, UPDRS part 3 (total), Hoehn and Yahr scale, before and 6 months after surgery, with electrical treatment alone, were analyzed retrospectively using multivariate analysis (ANOVA2).

Results: We found ($p < 0.05$) that walking and freezing worsen with partial coverage of left FF, whereas falls were increased if the contact doesn't cover left FF, whatever the coverage of right FF. The Hoehn and Yahr scale improved of 24.2% with a partial or a total coverage of left FF ($p < 0.05$).

Conclusions: It seems that FF is involved in SI gait disorders, in particular within the left hemisphere during bilateral chronic stimulation. This could be related to white matter tracks, located within the FF, that connect forebrain - basal ganglia and tegmentum implicated in locomotion.

4/OR04

LOCAL FIELD POTENTIALS OF THE SUBTHALAMIC NUCLEUS IN IMPULSE CONTROL DISORDERS IN PARKINSON DISEASE.

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Objetives: Dopaminergic treatments in Parkinson disease (PD) may be associated with motor and behavioral side effects. The motor complication includes fluctuations and levodopa induced dyskinesias (LID), and impulse control disorder (ICD) and dopamine dysregulation syndrome (DDS) as behavioral complications. In this presentation we study the oscillatory activity of the STN recorded through the electrodes implanted for DBS-STN in patients with ICD.

Material and Methods. 28 patients with chronic advanced PD have been operated in our department. We classified the patients in three different groups

- 1) Patients with ICD without LID (10 patients)
- 2) Patients with LID without ICD (9 patients)
- 3) Patients without LID neither ICD (PD controls) in whom the surgery was indicated because freezing or gait or severe motor fluctuations (9 patients).

In whole patients UPDRS-III, PD Impulse compulsive Questionnaire (QUIP) was assessed in each case and levodopa equivalents dose was calculated. After surgery STN local field potentials were recorded in "off" and "on" condition. We analysed postoperatively contact placement in correlation with the AC-PC line.

Results: STN recordings were analysed in "off" condition showing the spectrum of Beta range, one low beta-band (12-20 Hz) and other high beta-band (20-30 Hz). In "on" clinical condition the ICD patients showed an oscillatory activity theta-peak with a frequency of 6.71 Hz in the most ventral contacts. LID patients showed an oscillatory activity theta range of 8.38 Hz in the most dorsal contacts. PD control patients (No ICD neither LID) did not showed a oscillatory theta activity.

Coherence analysis showed that ventral oscillatory activity is correlated with frontal cortex activity while LID is recorded in motor area.

Conclusion: The STN is implicated in the motor and no motor complications of the dopaminergic chronic treatment trough a specific activity taking place in different anatomo functional territories.

5/OR05

BILATERAL DEEP BRAIN STIMULATION (DBS) OF THE GLOBUS PALLIDUS INTERNUS IN PRIMARY DYSTONIA USING AN OCTRODE (EIGHT-POLAR) LEAD – PRELIMINARY RESULTS

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Objective: DBS is an established method for the treatment of medically refractory dystonia. We aim to assess the feasibility of offering DBS by an eight-contact lead for treating the symptoms of medically refractory primary dystonia.

Methods: This is a single-center pilot study. Only patients who met stringent-criteria for refractory primary dystonia were recruited. Eight-polar DBS leads were implanted in the Globus Pallidus internus (GPI) using CT/MRI fusion-guided stereotactic localization. Dystonia symptoms were evaluated preoperatively and postoperatively using standard assessments, which included the Burke-Fahn-Marsden (BFMDRS) and the Unified Dystonia Rating Scale (UDRS).

Results: To date, 8 patients with primary generalized dystonia have been implanted with the 8-polar electrode DBS lead (7 bilateral and 1 unilateral). Two patients have been evaluated post-operatively at month 6, five patients at week 8 and one patient at week 4. At 8 weeks post-operative, the BFMDRS score improved from a mean of 33.2 ± 15.3 before surgery to a mean of 20.1 ± 16.5 , a 39.5% reduction. The UDRS score improved from a baseline mean of 48.3 ± 22.7 to a week 8 post-operative mean of 33.1 ± 26.8 , a 31.5% reduction. Updated results on all subjects will be presented along with examinations of quality of life and cognition.

Conclusions: These results suggest that DBS to the GPI using an 8-polar lead is an effective intervention in selected patients with primary generalized dystonia. Potential advantages of this particular type of 8-polar electrode versus the conventional 4-polar electrode in dystonia will also be discussed.

ORAL POSTERS

1/OP01

EFFECT OF GLOBUS PALLIDUS INTERNUS (GPI) AND/OR PEDUNCULOPONTINE NUCLEUS (PPN) DBS ON POSTURE AND GAIT IGNITION IN ADVANCED PARKINSON´S DISEASE

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Background and Aims:

To assess the effect of deep brain stimulation (DBS) of GPI and/or PPN on posture and gait ignition in advanced Parkinson´s Disease (PD).

Methods:

A 66-years old man with PD and motor fluctuations including severe peak-dose dyskinesia, on-freezing, and postural instability underwent bilateral GPI and PPN DBS. In best medical on, posture while level walking and gait ignition while turning on the spot were examined using clinic gait analysis (Vicon Motion System Ltd, Oxford, UK) with GPI DBS only (bipolar, 3,0V, 210µs, 130 Hz), with PPN DBS only (bipolar, 2,5 V, 60µs 25 Hz), and with combined GPI/PPN DBS. Posture was assessed by the upper body tilt angle (UBTA) in left-right body side for stance phase; to depict gait ignition, maximal rotational angle while turning on the spot (MaxRAWTOTS), mean time for turning 45° (MTT45) and the range of motion for the centre of mass while turning (ROMCOM) were measured.

Results:

	UBTA [°]	MaxRAWTOTS [°]	MTT45 [s]	ROMCOM [mm]
PPN DBS only	22,3	59	7,2	62
GPI DBS only	22,3	29	8,1	200
PPN and GPI DBS	16,1	217	1,7	37

Conclusions

Isolated GPI and PPN DBS had a similar impact on posture, but the combination of both significantly improved the upright posture. Gait ignition was worst with isolated GPI DBS and better with isolated PPN DBS. Again the combined stimulation yielded the biggest benefit. This combined approach may be useful in treating drug-resistant features of advanced PD and encourages future studies.

2/OP02

IMPROVING TARGETING ACCURACY IN IMAGE-GUIDED FRAME-BASED DEEP BRAIN STIMULATION

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Objective:

This study examines systematic errors in image-guided deep brain stimulation (DBS) electrode placement using the Leksell frame and explores a calibration strategy for stereotactic targeting.

Methods:

Pre and postoperative stereotactic MR-images were analyzed in 165 patients. The perpendicular error between planned target coordinates and electrode trajectory was calculated geometrically for all 312 DBS electrodes implanted. Improvement in motor UPDRS-III subscore was calculated for those patients with Parkinson's disease (PD) with at least 6-months of follow-up after bilateral subthalamic DBS.

Results

Mean(SD) scalar error of all electrodes was 1.4(0.9)mm with significant difference between left and right hemispheres. Targeting error was significantly higher for electrodes with coronal approach angle (ARC) $\geq 10^\circ$ ($P < 0.001$). Mean vector error was X:-0.6, Y:-0.7 and Z:-0.4mm (medial, posterior and superior directions respectively). Targeting error was significantly improved by using a systematic calibration strategy based on ARC and target hemisphere (mean: 0.6mm, $P < 0.001$) for 47 electrodes implanted in 24 patients. Retrospective theoretical calibration for all 312 electrodes would have reduced the mean (SD) scalar error from 1.4(0.9)mm to 0.9(0.5)mm (36% improvement). With calibration, 97% of all electrodes would be within 2mm of the intended target as opposed to 81% prior to calibration. There was no significant correlation between the degree of error and clinical outcome from bilateral STN DBS ($R^2 = 0.07$).

Conclusions

This study demonstrates that, after calibration of a systematic targeting error, an MR image guided stereotactic approach would be expected to deliver 97% of all electrodes to within 2mm of the intended target point with a single brain pass.

3/OP03

SIDE EFFECTS OF STN DBS IN PARKINSON DISEASE ARE THERE MORE FREQUENT WHEN PERFORMED UNDER CONTROLLED GENERAL ANESTHESIA ? A PROSPECTIVE SERIES OF 201 PATIENTS WITH LONG TERM FOLLOW UP.

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In order to evaluate, in Parkinson disease STN DBS the impact of general anesthesia on the frequency of side effects we have organized a prospective clinical trial.

Methods: Between January 2000 and February 2010, 241 consecutive parkinsons underwent implantation of bilateral electrodes in the STN. Postoperatively clinical assessments were done at 3,6,12, 36 and 60 months. During frame application and neuroimaging patients were under Propofol. At the operating room, the propofol was replaced by a combination of halogenated gas and Alfentanil. Concentration of halogenated were reduced to the lowest level possible at the time of recording. MR imaging includes a CISS ventriculography for indirect targeting, a coronal spinecho for direct visualization of the STN and a 3DT1 for sulci, ventricle and vessels avoidance. On 4-5 microelectrodes passive movement-related cellular activities were monitored, stimulation determined the level of intensity for capsular side effect and sometime allowed testing the positive effect on rigidity.

Results: A follow up longer than 1 year is available for 201 patients, more than 3 years for 89 patients and more than 5 years for 63 patients. The GA lasted seven hours (6-10) and the bilateral surgical procedure duration was about 4 hours. The STN was seen in all patients, typical STN and SN signal were recorded on 1-5 microelectrodes and the final implantation was on central position in 65%. Postoperatively 1 patient had an hemorrhage with permanent frontal syndrome, 1 had a severe pulmonary embolism with good outcome, 1 had an infection (requiring temporary removal of the devices reimplanted one year later with good result) and 1 had a transient confusion and one patient attempted suicide. At one year the improvement of the motor score was 60 %, axial score 42%, activities of daily living 36%, dyskinesia 73% and the motor fluctuations almost 63%. Dopaminergic treatments were significantly reduced (47%). Cognitive assessment and Beck were stable. Quality of life (PDQ39) was improved especially on the physical items.

Conclusion : Long term efficacy of STN-DBS under GA is in accordance with the main series using local anesthesia. However, this variant procedure requires a strict specific anesthesia with a comprehensive monitoring during each phase.

4/OP04

DTI STUDY OF SUBTHALAMIC NUCLEUS CONNECTIVITY IN PARKINSON'S DISEASE.

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Objectives: To study the connectivity of subthalamic nucleus in Parkinson's Diseases patients with DTI.

Patients and methods: We get DTI images with 3T MRI. We process these images with Volumen-One software (DTV.II SR toolbox, Tokio University). Our coordinates to locate subthalamus were 11mm. lateral, 3mm posterior, and 5 mm. lower, with a correction factor to be transfer to volume-one.

Our analysis volume was 3.8 mm (sensitivity FA 0.05 y ADC 0-3 and S 0-900). We study the tracts from the target in axial, saggital and coronal plane.

Results: We include 10 patients. DTI show that connectivity of subthalamic nucleous is with motor cortex, basal ganglia (thalamus, pallidum, and nigra) and descended connections (cerebellum and pedunculopontine nucleus).

Conclusions: Our results are similar to anatomical animal studies, except in tract to cerebellum. This connection was found previously in normal subjects, it could be cerebellum-thalamus tract. This resemblance permit to stablish the integrity of connectivity of subthalamic nucleus in Parkinson's disease.

5/OP05

STUDY OF POST-ACTIVATION DEPRESSION IN NORMAL SUBJECTS AND PARKINSON'S PATIENTS

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OBJECTIF : Rigidity is a cardinal symptom of Parkinson disease in which motoneurone responses to muscle afferent volleys are involved since it is suppressed after dorsal root section. In healthy subjects, motoneurone responses muscle afferents exhibit a frequency related depression: the greater the stimulus rate, the smaller the motoneurone responses. We investigated this frequency related depression in Parkinsonian patients undergoing deep brain stimulation.

METHOD : Flexor carpi radialis and Soleus H reflex were studied in 9 parkinson' s disease patients and 10 healthy subjects. Amplitude of the H reflex every 8seconds (H8) was compare to the aplitude of the H reflex every two seconds (H2). The ratio H2/H8 is correlate to the post-activation depression.

RÉSULTS : When the neurostimulation was OFF, the frequency related depression was completely suppressed and the patient rigid. When the neurostimulation was ON, the level of frequency related depression was restored and the rigidity almost suppressed.

DISCUSSION : These results strongly suggest that frequency related depression is controlled by descending pathways, whereas up to now, it was considered as relying only on local synapse mechanisms. We interpret this unexpected finding, taking into account the capacity of neuromodulatory input originating from the brainstem to boost spinal motoneurone firing.

CONCLUSION : Finally, although it may be argued that a neuronal circuit revealed in chronic patients may be not functional in healthy subjects, the present results strongly suggest for the first time in humans, that neuromodulatory inputs originating from brainstem influence the behaviour of spinal motoneurones.

6/OP06

DEEP BRAIN STIMULATION (DBS) OF THE POSTERIOR SUBTHALAMIC AREA AND VERBAL FLUENCY

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Introduction: Previously, we reported a mild transient dysphasia in 22.5 % of 40 patients after DBS in the posterior subthalamic area (PSA). We hypothesized that this was a micro-lesional effect, since it occurred before the stimulation was initiated. In order to evaluate these findings, we analyzed verbal fluency before and after surgery.

Methods: 16 consecutive patients with essential tremor operated with PSA DBS were evaluated off-stimulation regarding verbal fluency pre- and 3 days post-op. 10 patients were also tested after one year. 12 patients had left-sided, 3 had right-sided and 1 bilateral DBS. The tests used were time-dependent word naming tests.

Results: The mean number of words was 22.8 before surgery, which 3 days after the procedure was reduced to 17.4 (23.7%). After one year the scores were 24.5 and 19.3 (21.2%) respectively. The reduction in verbal fluency did not reach significance neither at the evaluation after 3 days ($p=0.08$), or after one year. The effect was however pronounced in individual cases with a reduction of up to 48.8 % after one year.

Conclusion: Previous studies have indicated reduced verbal fluency after STN and Vim DBS. Although there was a reduction, the difference did not reach significance in this small population evaluated after PSA DBS.

INTRAOPERATIVE MONITORING

ORAL PRESENTATIONS

1/OR06

OUR APPROACH TO SUBCORTICAL STIMULATION DURING RESECTION OF GLIOMAS IN ELOQUENT AREAS OF BRAIN

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Objective

The involvement of subcortical structures in the intrinsic tumors localized in eloquent areas require application of proper methods to detect them intraoperatively .

Methods

Between 1996 and May 2009, 153 patients (41 LGG, 67 HGG) had undergone surgery for lesions localized in eloquent areas during which intraoperative direct electrical stimulation of cortical and subcortical sites was performed. Involvement of subcortical structures by the intrinsic tumors emphasize the necessity of fiber tracking. There was applied real-time direct electrical stimulation by our specially designed bipolar probe which allowed to perform stimulation during debulking of the tumor. This gives immediate information of the position of the tracts involved in movement and speech. The train or/and continuous mode of stimulation implementing MEP was used.

Results

The intraoperative navigation gave advantage of tailored craniotomy and possibility navigate electrode during the resection of tumor and respecting results of direct electrical stimulation define the resection boundaries. Transient postoperative neurological worsening was observed in 34% of patients, which improved within 3 months in 93 % of them.

Conclusion

Removal of the tumor in the eloquent areas of the brain can be safely managed if the instrument for debulking has possibility simultaneously stimulate surrounding tissue to identify structures we are to avoid. It may help to maximize resection and preserve function.

2/OR07

SPINAL CORD STIMULATION PLACEMENT GUIDED BY INTRA-OPERATIVE CENTRAL H-REFLEX

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Introduction:

Placement of spinal cord stimulators (SCS) typically has required interaction with the patient during the procedure. Due to the analgesic and cognitive effects of general anesthetics (GA) and patient discomfort the responses can be unreliable. We developed an intraoperative neurophysiologic methodology, which uses the dorsal column as the signal pathway, to lateralize and appropriately localize the spinal cord electrode under GA.

Methods:

Needle electrodes are placed bilaterally in 5 to 6 limb muscles for continuous EMG recording. SCS stimulation parameters are: 60 Hz and 210 μ Sec. Voltage or current is raised until active EMG is noted. Unilateral as well as bilateral thresholds are noted. Multiple contact combinations along the perimeter as well as the center of the electrode are tested to map out the midline of the spinal cord and the electrode relationship to the pain pattern. In 15 of the patients, collision studies (between the SCS stimulation and the standard H-reflex test) and/or paired pulse analysis was performed to evaluate the pathways activated using this technique.

Results:

70 patients (46 female mean age of 52.2 ± 14.6) had paddle leads implanted over an 18 months period. Lateralization was achieved in all 70 patients. 6 of the patients demonstrated no pain relief post-op while 3 demonstrated less than 50% pain relief. The other 61 patients demonstrated 50% or greater relief. Intraoperative collision studies confirmed the dorsal columns as the signal pathway generating the EMG activity, similar to a standard H-reflex.

Conclusion:

This data supports using EMG/H-reflex testing under GA for safer, more comfortable, paddle lead placement. This specific methodology utilizes the same anatomic pathways as those thought to mediate benefits using SCS.

3/OR08

NONLINEAR NEURONAL FIRING PATTERNS OF SINGLE UNIT ACTIVITIES OF GLOBUS PALLIDUS EXTERNAL AND INTERNAL IN DYSTONIA.

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Objective: The aim of this study was to evaluate the variability of non-linear neuronal discharge patterns between the external and internal segments of the globus pallidus (GPe and GPI) in patients with dystonia.

Methods: Twenty dystonia patients were studied during functional stereotactic neurosurgical operations for implantation of deep brain stimulation (DBS) electrodes. There were 11 men and 9 women, mean age at surgery was 44 ± 3.7 years. Diagnosis were generalized dystonia (6 patients), cervical dystonia (8 patients) and segmental dystonia (6 patients). In 2 patients surgery was performed under general anaesthesia while 18 patients had local anaesthesia only without sedation or analgesic medication. Single-unit activity recordings in the GPI and GPe were obtained during routine microelectrode recording and mapping to delineate nuclear borders and to identify the sensorimotor subregions.

Results: Based on comparison of standard deviations, coefficient of variation and dispersion index, ISIs from cells recorded in the GPI were shorter and less variable than ISIs from GPe cells. By using approximate entropy (ApEn), a nonlinear feature of statistical analysis, it was demonstrated that the ApEn values in most cells of the GPe were lower than of those in the GPI. Our data indicate that in the majority of cells i.e. 18/22 (82%) in the GPI and 5/5 (100%) in the GPe for 1000 ISIs, raw ISIs have lower entropy values than those observed after resampling of the original series.

Conclusions: This study indicates non-linear temporal organization as a common feature of neuronal discharge probability distribution in both the GPe and GPI of patients with dystonia.

4/OR09

SIGNAL TO NOISE VARIATIONS IN AXONS STIMULATED BY DBS

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Problem:

The firing rate output of axons connected to active cell bodies and also within the stimulation field of an active Deep Brain Stimulating (DBS) electrode was studied to help understand the changes in functional axonal output when the DBS signal is added to aberrant cell firing noise.

Background:

In many modes of Deep Brain Stimulation (DBS) the external applied signal (stimulus pulse) generates action potentials that propagate bi-directionally along the activated axon. These new coherent action potentials end in one of three ways: (1) by activating the synaptic terminals of the axons; (2) hitting the axon hillock and degrading; (3) colliding with a cell body generated action potential (which we define as the noise signal). The amount of noise that passes is a function of the axonal length, diameter, and stimulus frequency. Knowing this may be helpful is assessing information transfer between basal ganglia nuclei (BG) and between BG and other areas of the brain.

Methods:

Both a theoretical model and computer simulations (using UNCuS – an in house neural circuitry simulator) were performed. In order to assure that the effects of axonal geometry were included in the model the maximum activating function was employed and a special 3-D axonal modeling system was added to the software, thus any bending, where the activating function influence is greater, was included.

Results:

A equation was determined that related the signal to noise ratio as a function of the stimulation frequency (f_a), the average output rate of the cell (f_c), the location of the maximum activating function ($L_{\max AP}$), the action potential propagation velocity (V_{AP}) (which is a function of diameter and myelination) and the refractory time of the axon (T_r) (see equation below).

$$SNR = \frac{f_a}{\bar{f}_c \left[1 - 2f_a \left(\frac{L_{\max AP}}{V_{AP}} + T_r \right) \right]}$$

Conclusion

A key finding of this study is that it is not only important to use a DBS signal that is of the correct frequency to functional be important, but the signal frequency needs to be high enough collide to with an appropriate number of aberrant pulses to "re-normalize the system". More studies are also needed to determine what that normalized pulse sequence should look like.

5/OR10

CONCEPT OF BRIDGING THE LESION CAVITY WALL WITH STIMULATING AND RECORDING DEVICES IN THE CENTRAL NERVOUS SYSTEM

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6/OR11

A NORMALIZED PER-OPERATORY MICROSTIMULATION MAPPING OF THE ROSTRAL BRAINSTEM AS A TOOL TO DELINEATE PPNa TARGET

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In severe Parkinsonism, DBS of the PedunculoPontine Nucleus area (PPNa) has been proposed to treat freezing of gait. Preliminary results are promising but the efficacy of PPNa-DBS remains heterogeneous. One possible explanation is that precise localization of the best target has not been established yet. Per-Operative Microstimulations (POM) remain a powerful feature to delineate PPNa surrounding structures and potentially the PPN *per se*. Using our Brainstem Normalized Coordinate System (BNCS) centered on PontoMesencephalic Junction (PMJ), we aimed to provide a precised mapping of the microstimulation-induced effects of the rostral brainstem and to underline the relevant effects at PMJ level for best clinical outcomes.

In 12 parkinson patients, 2 to 3 simultaneous trajectories per side, were performed representing a total of 57 trajectories. POM sites were established every 3mm from -5mm to -15mm below AC-PC plane. Stimulation parameters were : Frequencies : 25 / 130Hz ; Pulse width : 0,06ms ; Intensity : from 0.1 to 4mA.

We analysed microstimulation-induced effects in 252 different sites. Here we report and plot in a BNCS the three main side effects depending on frequency parameters : mono and binocular troubles at both 25 and 130Hz, myoclonia / muscular vibration-like at 25Hz and paresthesia mainly at 130Hz. Paresthesia at 25Hz and monocular troubles must be avoid. Best clinical outcomes were obtained when 130Hz POM induced only soft paresthesia on the contralateral face and upper limb and 25Hz POM induced myoclonia / muscular vibration at PMJ level that could be a relevant signature of the target.

7/OR12

DTI-TRACTOGRAPHY AND MRI ASSISTED SUBTHALAMIC ELECTROPHYSIOLOGICALLY-GUIDED TARGETING FOR DBS IN PARKINSON'S DISEASE

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Objectives: The aim of this study is to explore the feasibility of subthalamic nucleus (STN) targeting through indirect red nucleus (RN) visualization.

Methods: A group of 27 patients underwent STN DBS. T2 images were used to localize the STN and RN and Diffusion Tensor Imaging (DTI) to identify tracts responsible for side-effects as internal capsule (IC), medial lemniscus (ML), frontal eye field connections (FEF) and III cranial nerve (IICN).

The coordinates of the final position of electrodes following microrecordings with positive clinical response were placed in a 3D volumetric reconstruction of the STN through indirect RN imaging divided in six quadrants, including the active contacts with associated side-effects, like tonic muscle contractions, paresthesias, skewed and conjugate eyes deviation, the distance to the corresponding tract being calculated.

Results: RN visualization and volumetric reconstruction of STN and tracts were achieved in 22 out of 27 cases. The final coordinates of the electrode with motor symptoms improvement were located in the dorsoanterolateral area of the STN in 66% of cases. The mean distance between the active electrodes and the tracts responsible for side-effects were 2.34, 4.16, 4.98 and 0.6 mm for the IC, ML, FEF and IICN respectively.

Conclusions: Our results may support in the next future the shift from electrophysiologically-guided image-assisted to a new image-guided electrophysiologically-assisted DBS.

ORAL POSTERS

1/OP07

VOICE ACOUSTIC ANALYSIS IN DETECTION OF OVERSTIMULATION DURING BILATERAL SUBTHALAMIC STIMULATION IN PARKINSON'S DISEASE

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The purpose of this study was to investigate the effects of bilateral subthalamic deep brain stimulation on the phonation of patients with Parkinson's disease (PD) and to detect the overstimulated condition upon voice acoustic changes.

Conversational speech and sustained vowel sounds /a/, /i/, high /i/, /o/ and /u/ of 22 PD patients were recorded on a computer hard disk in 3 conditions: (1) after a 12-hour withdrawal of all antiparkinsonian drugs with a turned off stimulator (OFF); (2) with optimal bilateral stimulation (ON); (3) with an overstimulation on the same site while the amplitude was increased by 20-30% (OVER). The most stable phonatory 6-second window was selected for acoustic analysis from each of the sustained vowels. Perturbation jitter, shimmer and noise-to-harmonics ratio (NHR) and nonlinear dynamic analysis (NDA) parameters (detrended fluctuation and recurrence period density entropy) were compared and entered for quadratic discriminant analysis (QDA) of conditions.

NDA showed more significant changes and more powerful correlation with perceptual scores than perturbation measures. The highest correct classification percentage during QDA within vowels was observed with parameters of NDA. At the OFF-ON discrimination the total correct classification rate ranged from 83.2 to 90.6%, with the best performance during /o/ and /u/. The ON-OVER QDA with nonlinear values showed from 78.4 to 93.8% of correct classification rate with best results during /i/.

Acoustic voice analysis helps in recognizing the overstimulated condition, and with an appropriate acoustic test battery including NDA can be a useful tool for fine adjustment of stimulation parameters.

MOVEMENT DISORDERS II

ORAL PRESENTATIONS

1/OR13

DORSAL STN DBS ALLEVIATES PD GAIT DEFICIENCIES MORE THAN VENTRAL STN DBS

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Background: Deep brain stimulation (DBS) of the subthalamic nucleus (STN) alleviates Parkinson's disease (PD) symptoms (tremor, rigidity and bradykinesia) and may improve gait and postural impairment associated with the disease. However, improvement of gait is not always as predictable as the clinical outcome. This may relate to the type of gait impairment or localization of the active DBS contact.

Methods: Quantitative gait analyses based on 3D motion-capture were performed in 10 PD patients, treated with bilateral STN DBS. The active contact was visualised on peri-operative MRI. Stimulation sites were grouped as either in the dorsal/ventral STN or medial/lateral hereof and anterior/posterior STN or medial/lateral hereof. The localization was compared with clinical improvement (UPDRS-III) and gait performance OFF and ON STN DBS, off medication.

Results: 17 of 20 active contacts were located within STN borders, 14 in the dorsal half. Step velocity and -length improved significantly more with dorsal stimulation compared with ventral stimulation ($p=0.03$ and $p=0.02$). Parameters of balance during gait were also more improved with dorsal stimulation compared with ventral stimulation. Dorsal STN DBS improved contra-lateral UPDRS-III more than ventral STN DBS ($p<0.05$).

Conclusion: DBS of the dorsal STN is superior to stimulation of the ventral STN. The outcome of STN DBS on overground walking may depend on STN stimulation site. This may relate to topographic arrangements of STN connections. Possibility of differences in outcome dependent on stimulation site underlines the need for exact knowledge of the active stimulation site in order to target the most effective area.

2/OR14

OBSERVER BIAS IN BIO-SURGICAL TRIALS OF NOVEL PARKINSON'S DISEASE THERAPIES

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Background/Objective: Six times in the last 10 years, a surgically administered biological therapy for Parkinson's disease (PD) that appeared to be effective in an open-label feasibility trial (OLT), failed to generate similar results when tested subsequently in a prospective, double-blind sham surgery-controlled trial (SSCT). The prevailing consensus is that these false positive results were caused by strong placebo responses. The goal of this study was to test that hypothesis.

Methods: Retrospective review of the clinical responses reported from both the initial OLT and subsequent SSCT of these six 'bio-surgical' therapies. When available, the off medication Unified Parkinson's Disease Rating Scale Motor Sub-score (UPDRS-III) was recorded so that clinical responses could be compared across trials.

Results: Direct comparisons of the OLT and SSCT responses could be made for four of the six therapies. In three of these four instances, the clinical response to the active therapy was reduced >50% in the SSCT as compared to the OLT. The mean response to therapy averaged 36.6% in the OLTs vs.15% in the SSCTs. The mean placebo response was just 11%. Moreover, significant adverse events emerged during the SSCTs that were not observed during the OLTs.

Conclusions: Observer bias was a stronger factor than placebo effect in yielding these Type I errors. Open-label trials with less than 12-15 subjects are insufficient to determine if a bio-surgical PD therapy should proceed to Phase II/III sham-surgery controlled trials. Instead, Phase I trials should be blinded and include untreated controls.

3/OR15

IMPROVEMENTS OF MOTOR SYMPTOMS IN ADVANCED PARKINSON'S DISEASE (PD) PATIENTS TREATED WITH EPIDURAL MOTOR CORTEX STIMULATION (EMCS)

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Objectives

Epidural motor cortex stimulation (EMCS), usually performed unilaterally, is a minimally invasive stereotactic procedure recently employed in advanced Parkinson's disease (PD). It might be a valuable therapeutic option for patients with advanced Parkinson's disease (PD) who can not be treated with DBS.

METHODS:

EMCS consists of the epidural installation of a quadripolar electrode over the primary motor cortex, contralaterally to the most suffering side. Nine patients underwent an unilateral implant while two have been implanted bilaterally. All patients could not be addressed to DBS for the advanced age, for the presence of cortical atrophy and cognitive impairment or for poor response to the levodopa therapy. Stereotactic frame based image-guided localization of the target was employed to provide a precise placement. CT-MR fusion was performed pre-operatively for target planning and post-operatively to confirm proper electrode placement. Patients were assessed preoperatively and 1, 6 and 12 months after surgery, on (med ON) and off (med OFF) medications, with stimulator on (stim ON), and 2 weeks later with stimulator off (stim OFF).

RESULTS

All patients improved significantly after implant; at 1 month of stimulation patients had a significant improvement of UPDRS Part II, Part III and OFF- duration. In med OFF stim ON condition UPDRS II score decreased significantly. The mean improvement of this scale was around 17% constant at each control visit. In the same condition also UPDRS III decreased significantly after 1 month (41.25 ± 9.42) of stimulation and the decrease stayed stable. Motor aspect mean improvement was around 15% during the follow up period. Also OFF period score showed a significant with a mean improvement of 30%. In med ON stim ON condition, data showed an improvement in UPDRS part II after 1 month of stimulation the mean percentage of improvement was 23.5% in the follow up period. UPDRS part III decreased significantly just after a month of stimulation the mean improvement of this scale was 15%. In med ON stim ON condition, Off duration showed the same characteristics: a significant decrease which was constant for all study period with a mean improvement of 35%. The mean total levodopa equivalents were significantly reduced after one year of stimulation (-34%). The procedure was not associated with surgical complications or stimulation-related side effects.

Conclusion

We found that motor cortex stimulation is a safe minimally invasive surgical procedure well tolerated from all patients. We observed modest motor benefits after both unilaterally both bilaterally EMCS, and a reduction of daily medication dosage and involuntary movements more pronounced after bilaterally implant.

ABNORMALITIES OF BRAIN ARCHITECTURE IN PARKINSON'S DISEASE: A STATISTICAL DIFFUSION TENSOR NEUROIMAGING ANALYSIS

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Introduction

Parkinson's disease (PD) is a progressive neurodegenerative disorder affecting up to 2% of the population over the age of 65. PD encompasses a variety of motor symptoms, characterized by tremor, rigidity and bradykinesia. We investigated brain abnormalities in structure and connectivity in a cohort of PD patients who received Deep Brain Stimulation (DBS) treatment, using new diffusion tensor imaging techniques.

Methods:

PD patients (n=28) and control subjects (n=24) with no history of neurological diseases or symptoms were enrolled prospectively. Diffusion weighted data was acquired using echo planar imaging, (isotropic voxel size 2mm; 32 directions of diffusion weightings). Voxelwise statistical analysis of the fractional anisotropy (FA) data was performed using tract based spatial statistics. FA images were generated by fitting a tensor model. A mean FA image was created and thinned to establish a mean FA skeleton. Stereotactically aligned FA data was projected onto this skeleton and the resulting data passed into voxelwise cross-subject statistics, using a permutation-based inference tool for nonparametric statistical thresholding.

Results:

Tract-based spatial statistical analysis demonstrated reduced FA in various motor and non-motor pathways in PD. Reduced FA was demonstrated in the corpus callosum ($p<0.01$), corona radiata and corticospinal tracts ($p<0.01$), fronto occipital fasciculus, forceps major ($p<0.02$), superior longitudinal fasciculus ($p<0.05$), and subcortical white matter of the supplementary motor area (SMA) ($p<0.02$). Further voxelwise analysis of grey matter and white matter FA demonstrated reductions of FA in the posterior limb of the internal capsule and the thalamus.

Conclusions:

Using computational analytical tools this study has demonstrated abnormalities of fractional anisotropy in a cohort of non-dementia, motor predominant PD patients. Reduced FA is thought to represent a loss of integrity of neuronal tissue. This was evident in known motor pathways in PD including subcortical white matter of the SMA, thought to be involved in the planning of motor actions. However non-motor pathways also demonstrated abnormalities including those of the prefrontal area. These findings may help elucidate aspects of the complex pathophysiology of PD, and may be applied as a tool in patient selection for DBS.

5/OR17

PALLIDAL DEEP BRAIN STIMULATION MAY INDUCE PARKINSONIAN GAIT DISORDERS IN PATIENTS WITH FOCAL AND SEGMENTAL DYSTONIA

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Objectives: Deep brain stimulation (DBS) of the globus pallidus internus (GPi) has been shown to be an effective treatment for patients with medically refractory segmental and generalized dystonia. Recently, stimulation-induced bradykinesia or parkinsonism have been reported as rare side effects of chronic DBS of the GPi. The aim of this study was to better delineate parkinsonian gait disorders with chronic GPi DBS.

Methods: We retrospectively screened our data base of dystonia patients who underwent DBS of the posteroventral GPi in the period between 2000 and 2010. Those who spontaneously reported a newly emerged gait disorder after DBS were included into this study.

Results: A total of five patients were identified. All of them had significant benefit from DBS with regard to the suppression of dystonia. After DBS, they described a gait disorder closely resembling freezing of gait (FOG): difficulties with initiation of gait, shuffling steps, having their feet glued to the ground. FOG vanished within minutes after turning off DBS. In one patient, by reducing the frequency from 130 to 60 Hz dystonia was well controlled without the recurrence of FOG; in the other 4 patients a compromise between improvement of dystonia and stimulation-induced adverse effects was made.

Conclusion: A stimulation-induced FOG-like gait disorder following GPi DBS may develop in a subset of patients with focal and segmental dystonia. In all cases, a compromise between treatment of dystonia and FOG was achieved.

6/OR18

IS BILATERAL PALLIDAL DEEP BRAIN STIMULATION NECESSARY IN CERVICAL DYSTONIA?

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Introduction: Focal cervical dystonia is a disabling condition. Bilateral pallidal deep brain stimulation (DBS) has been successful in treating this condition. There are some reports of patients requiring only unilateral DBS for cervical dystonia. The potential benefits to the patient are that it reduces operative time and risk and reduces the frequency of replacing exhausted implantable pulse generators.

Objectives: To determine if pallidal DBS ipsilateral to the affected sternocleidomastoid, is sufficient to treat cervical dystonia.

Methods: Patients who have had bilateral pallidal DBS to treat cervical dystonia were randomised to either have their systems turned off ipsilateral to the direction of head turning or left alone. Patients were blinded to this intervention and were reassessed with TWSTRS scores before crossing over to the alternate arm of the trial.

Results: All 3 patients had increasing pain and cervical dystonia within 2 weeks when the pallidal stimulator ipsilateral to the direction of head turning was switched off. Each of their TWSTRS scores worsened from baseline as follows: 21 to 29.25, 7.25 to 29 and 14.5 to 31.25.

Discussion: In humans, sternocleidomastoid is believed to be innervated by the ipsilateral hemisphere although this is controversial. In patients with torticollis, pallidal DBS ipsilateral to the involved sternocleidomastoid alone is not as effective as bilateral pallidal DBS. Other contralaterally innervated neck muscle involvement may account for the persistent dystonia. Patients who have hemidystonia with neck involvement may only require unilateral DBS and consideration should be given to initially placing unilateral pallidal DBS in these cases.

7/OR19

**ACCURATE TARGETING OF THE PEDUNCULOPONTINE NUCLEUS
BY AN MRI-GUIDED APPROACH - A CADAVER STUDY**

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Objective:

Clinical studies on pedunclopontine (PPN) deep brain stimulation (DBS) have been adversely affected by difficulties in visualizing the nucleus on MRI. This study examines the anatomical accuracy of a clinically relevant MRI protocol for stereotactic targeting of the PPN in a human cadaver.

Methods

Approval for the study was obtained from the local Research Ethics Committee. After attachment of a Leksell frame to a cadaver head (male, age-at-death 68y), direct MRI-localization, stereotactic targeting of PPN and final electrode confirmation was performed using a previously published proton-density protocol at 1.5T (2mm-thick contiguous slices; TR/TE:4000/15ms; echo-train:7; NEX:3; BW:15.63kHz; FOV:250 mm; matrix:256x256; acquisition-time:7min). The brain was removed from the cranium and imaged utilising a high-field 9.4T VMRIS scanner (Varian Inc, Palo Alto, USA) after extraction of the electrodes. The specimen was then processed into paraffin blocks using routine protocols. Sections were stained with Luxol fast blue/cresyl violet or haematoxylin and eosin.

Results

High-field MR-images (9.4T) and low-power histological images revealed a persistent track in the intended PPN region as defined anatomically by the surrounding fibre tracts (medial to the lemniscal system and lateral to the central tegmental tract and decussating superior cerebellar peduncles). Histological examination also confirmed that the adjacent neuropil contained scattered large neurons consistent with the appearance of PPN neurons.

Conclusions

The results validate excellent accuracy with direct MRI-guided targeting of the visualized human PPN. This method also serves to document electrode location and would therefore appear to be of relevance to groups evaluating the clinical role of PPN DBS.

ORAL POSTERS

1/OP08

SUBTHALAMIC DBS FOR PARKINSON'S DISEASE UNDER GENERAL ANAESTHESIA: CLINICAL RESULTS COMPARED WITH AWAKE SURGERY.

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Introduction: surgery for deep brain electrode implantation generally require clinical cooperation of the patient: for this reason, the patient should be awake, cooperative and – in case of Parkinson's disease surgery – free of drugs. Moreover, in some cases, it may be hard to obtain the patient's collaboration: stress, fear, drug washout and psychological profile of the patient may concur to make difficult an awake surgery. Few reports deal with DBS surgery under general sedation. While considering awake surgery like the "gold standard", we report the results obtained in a small number of patients operated for StnDBS under general anaesthesia, for different reasons.

Methods: 14 patients (6F, 8M, aging 53-65) out of 242 operated from 1998 to 2010 (sept) were included in the study. Patients requested general sedation for anxiety and self-evaluation to be un-cooperative during the awake surgery. Preoperative psychological and psychiatric balance confirmed the high anxiety grade of the patients. Surgery was under general anaesthesia (short action BZD and i.v. Diprivane); intraoperative monitoring was performed with MERs. Clinical assessment was performed at baseline and 2 years postoperatively, by means of UPDRS evaluation in both "on" and "off"-medication. L-dopa equivalent dosage, surgical and stimulation-related adverse events were also recorded.

Results: mean UPDRS III in "drug-off/stim-on" condition was 43 (± 13) pre-operatively, and 23 (± 7) at 2 year follow-up. Baseline L-dopa equivalent dosage was 1250 mg at baseline and 650 at 2 years. 2 patients experienced hypofonia/dysarthria, 1 had transient eyelid apraxia, 2 had stim-dependant paresthesias, 1 developed transient depression. There were no surgical complications.

Conclusions: StnDBS under general anaesthesia may be performed in carefully selected cases; medium term follow-up did not differ from awake surgery patients' one.

RHEUMATIC PAIN MAY IMPAIR THE EARLY OUTCOME OF DEEP BRAIN STIMULATION IN PARKINSON'S DISEASE.

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Object. To analyse postoperative rheumatic complaints in patients with Parkinson's disease (PD) submitted to bilateral subthalamic nucleus (STN) stimulation.

Methods. Fifty-three PD patients (mean age, 59.9 ± 8.3 years; mean disease duration, 11.5 ± 4.2 years) referred for STN stimulation were enrolled. Patients were prospectively asked to refer and describe any rheumatic pain they experienced at any time during the preoperative period and within the 6 postoperative months. Pre-existing rheumatic pain, therapeutic changes, parkinsonian motor disability and weight gain were assessed as explanatory factors for rheumatic pain occurrence after surgery.

Results. Thirty patients (57 %) complained of rheumatic pain whereas all demonstrated great functional improvement after surgery. Twenty (67 %) among the 30 experienced similar pain sensation before surgery. Symptoms occurred rapidly, between 4 and 26 postoperative weeks, while the preoperative treatment was reduced. Multiple stepwise regression analysis showed that pre-existing rheumatic pain, 6-month postoperative UPDRS III motor score and axial sub-score improvements in the *off-drug/on-stimulation* condition were accurate independent predictors of rheumatic pain after surgery ($F(8,41) = 2.20, P < 0.047$).

Conclusion. Our results highlight the high prevalence of rheumatic pain arising shortly after STN implantation. An accurate pain and osteo-articular assessment should be performed preoperatively in PD candidates for STN stimulation in order to limit emergence of complications in the early postoperative period.

3/OP10

SIGNIFICANT REDUCTION IN STEREOTACTIC AND FUNCTIONAL NEUROSURGICAL HARDWARE INFECTION AFTER LOCAL NEOMYCIN/POLYMYXIN APPLICATION.

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OBJECT: Hardware infection is a common occurrence after the implantation of neurostimulation and intrathecal drug delivery devices. The authors investigated whether the application of a neomycin/polymyxin solution directly into the surgical wound decreases the incidence of perioperative infection. METHODS: Data from all stereotactic and functional hardware procedures performed at the Oregon Health & Science University over a 5-year period were reviewed. All patients received systemic antibiotic prophylaxis. For the last 18 months of the 5-year period, wounds were additionally injected with a solution consisting of 40 mg neomycin and 200,000 U polymyxin B sulfate diluted in 10 ml normal saline. The primary outcome measure was infection of the hardware requiring explantation. RESULTS: Six hundred fourteen patients underwent hardware implantation. Among 455 patients receiving only intravenous antibiotics, the infection rate was 5.7%. Only 2 (1.2%) of 159 patients receiving both intravenous and local antibiotics had an infection. The wounds in both of these patients were compromised postoperatively: 1 patient had entered a swimming pool, and the other had undergone a general surgery procedure that exposed the hardware. If these patients are excluded from analysis, the effective infection rate using a combined intravenous and local antibiotic prophylaxis is 0%. There were no complications due to toxicity. CONCLUSIONS: The combination of local neomycin/polymyxin with systemic antibiotic therapy can lead to a significantly lower rate of postoperative infection than when systemic antibiotics are used alone.

4/OP11

OPTIMAL BASELINE TIMEPOINTS FOR ASSESSING THE STN-DBS IMPACTS IN PATIENTS WITH ADVANCED PARKINSON DISEASE

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Objectives: To re-appraise the optimal timepoint as baseline for assess the efficacy of STN-DBS in patients with advanced Parkinson's disease (PD).

Methods: Forty consecutive patients with motor fluctuations despite optimal medical treatment (median Hoehn and Yahr Stages 3 during the "drug-off" period) underwent bilateral STN-DBS surgery between May 2004 and April 2008. Patients were evaluated using the Unified PD Rating Scale (UPDRS) at 3-, 6- and 12-months after the surgery in "drug-off/DBS-on" state compared firstly to the preoperative value, then to value at each timepoints in "drug-off" state as baseline.

Results: Total mean daily levodopa-equivalent dose was reduced by 19/19/28% at 3-, 6- and 12 months, alternatively. The decreased amplitude of mean total/part II/part III UPDRS scores to the preoperative state were as following: $Y_{total} = 100\% - 27.5\%$ (if 3Mo, $p=0.001$) – 34.2% (if 6Mo, $p<0.001$) – 21.8% (if 1Y, $p=0.009$); $Y_{II} = 100\% - 28.8\%$ (if 3Mo, $p=0.006$) – 36.8% (if 6Mo, $p=0.001$) – 15.1% (if 1Y, $p=0.153$); and $Y_{III} = 100\% - 27.6\%$ (if 3Mo, $p=0.003$) – 33.8% (if 6Mo, $p<0.001$) – 25.9% (if 1Y, $p=0.003$). However, if based on each "drug-off/DBS-off" period, the improved rates at 12-month were by 25.8% ($p<0.0001$)/ 21.0% ($p=0.009$)/ 31.6% ($p<0.0001$), alternatively. These were closely to the real world.

Conclusions: Due to degenerative processing of PD over time, the "drug-off/DBS-off" value at each timepoint is the optimal baseline for evaluating the impacts of STN-DBS therapy.

5/OP12

LONG TERM EVALUATION OF BILATERAL DEEP BRAIN STIMULATION OF THE SUBTHALAMIC NUCLEUS IN ADVANCED PARKINSON DISEASE PATIENTS, FOLLOWED UP MORE THAN 5 YEARS.

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Introduction: Deep brain stimulation (DBS) of the subthalamic nucleus (STN) showed very strong effect to alleviate all of the motor symptoms in advanced parkinsonian patients in short-term period. Also several reports indicates its long term effects after 2 to 3 years. However, only few data are reported about its long-term effect more than 5 years. We studied the long-term results of 26 parkinsonian patients who underwent DBS of the STN and were followed up for more than 5 years after implantation of the DBS systems.

Methods: We underwent 116 STN-DBS surgery for advanced parkinsonian patients since 1998. Among these patients 26 were followed up more than 5 years. The longest follow up period was 11 years and 9 months. They were evaluated using Unified Parkinson's Disease Rating Scale (UPDRS) and Hoehn & Yahr stage. We also evaluated the medical problems and additional medication among these periods.

Results: Mean total UPDRS score of these patients improved from 78.4 (n=24) of preoperative period to 46.4, 58.8 and 60.4 immediately after the operation, 3 years and 5 years after the operation. Statistically significant improvement of the total UPDRS score compared to preoperative period remained 5 years after the operation. Patients' axial symptoms such as gait, speech and swallowing deteriorated after 3 years, whereas they showed continuous improvement about tremor, rigidity and wearing off. Non-motor symptoms of Parkinson disease, such as deterioration of cognitive function, hallucination and delusion, fluctuation of blood pressure became their major problems among 5 years after STN-DBS.

Conclusion: STN-DBS showed sustained improvement so-called dopamine-related motor functions, such as tremor or rigidity in Parkinson disease patients, but not for axial symptoms which was considered as non-dopamine-related motor functions. Also their major problems became non-motor symptoms, such as cognitive, psychological and autonomic disturbance 5 years after surgery. .

6/OP13

LONG-TERM FOLLOW-UP OF BILATERAL PALLIDAL STIMULATION IN PATIENTS WITH PRIMARY GENERALIZED DYSTONIA.

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Objectives:

Bilateral pallidal stimulation is an established management of patients with primary generalized dystonia (PGD). The aim of this study is to present our experience of bilateral pallidal stimulation in patients with PGD in the long-term follow-up.

Methods:

The study population is composed of 8 patients with the diagnosis of PGD (4 patients with DYT-1 positive PGD and 4 patients with DYT-1 negative PGD). The patients were operated on in general anesthesia because of severe dystonia and young patient's age. The stereotactic target - posteroventrolateral pallidum was calculated according to the midcommissural point derived from fusion of stereotactic computer tomography images with magnetic resonance images. The DBS leads (Type 3387) were implanted without intraoperative electrophysiological guidance. The formal objective assessment included the Burke-Fahn-Marsden Dystonia Rating Scale (BFMDRS). The BFMDRS assessment was performed before and after surgery. All patients completed 3 years postoperative follow-up.

Results:

At the last follow-up visit (3 years after surgery) in 4 patients with DYT-1 positive PGD the functional and motor parts of the BFMDRS improved by 45 % and 58 % respectively when compared to the preoperative scores. In 4 patients with DYT-1 negative PGD the functional and motor parts of the BFMDRS improved by 31 % and 43 % respectively. The hardware-related complications occurred in 3 patients (3 breakages of DBS leads). 2 breakages were located in the proximity to the burr whole cup and 1 just above connector. All hardware-related complications were successfully managed.

Conclusions:

Bilateral pallidal stimulation is an effective and safe treatment in patients with PGD. The incidence of hardware-related complications in PGD patients seems to be higher than in patients with Parkinson's disease.

7/OP14

EFFICACY OF VIM-DBS FOR MULTIPLE SCLEROSIS- RELATED TREMOR.

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Introduction.

Severely disabling complex tremor is common in multiple sclerosis (MS). The objective of this retrospective study was to evaluate the efficacy of thalamic ventrointermedius nucleus deep brain stimulation (Vim-DBS) in multiple sclerosis related tremor (MST).

Patients and Methods.

We retrospectively evaluated patients with MST, who had undergone VIM- DBS, between 2000 and 2009 at the WCNN-Liverpool. The pre and postoperative evaluations included standard tremor assessment using the tremor rating scale (TRS), video recording, health-related quality of life assessments using the SF-36 and Euroqol-5D questionnaires and Expanded Disability Status Scale (EDSS). In 4 patients the DBS was implanted using Neuromate robot (Integrated Surgical Systems, Lyon, France) and in 5 using the NexFrame (Medtronic Navigation).

Results.

9 patients with MST were treated with VIM-DBS. There were 4 males and 5 females, age range between 25-61 years. The mean duration of the diagnosis of MS was 9.6 years (2-27 years), and the mean duration of MST was 5 years (1-15 years). Follow-up ranged from 8 to 88 months (mean 37 months). Seven had bilateral VIM-DBS implantation whereas 2 had unilateral VIM-DBS. MS relapse was observed in 2 cases at 3 and 12 months postoperatively. Tremor control was achieved in all nine patients; 4 had good control and 5 had moderate control. Overall, there was statistically significant improvement in the postural component of the tremor ($p < 0.05$) and the total tremor score ($p < 0.05$). We did not find any statistically significant change in the EDSS pre and postoperatively. Similarly, the EQ-5D indices and the VAS scores did not reveal any statistically significant change following DBS implantation.

Conclusion.

VIM-DBS for MST is safe and associated with a low morbidity rate. Tremor reduction is commonly achieved postoperatively. Treatment goal needs to be individualised according to the initial neurological status

8/OP15

OUR EXPERIENCE IN NEUROMODULATION FOR MOVEMENT DISORDERS.

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OBJECTIVE: to analyse our results of bilateral subthalamic nucleus (STN) deep brain stimulation (DBS) for treatment of Parkinson's disease (PD) and GPi stimulation for patients with dystonia.

MATERIAL AND METHODS: 11 patients with PD and 4 patients with dystonia were operated on between 2008 and 2009 years with follow – up period from 6 months up to 2 years. In all cases the electrodes Medtronic Kinetra™- 3387 were implanted bilaterally into the STN or GPi using a Radionics CRW frame. An intra-operative microelectrode recording (MER) was performed in 5 cases, checking up to 3 trajectories at each side with microstimulation following by a neurological evaluation. The clinical rating tests included Unified Parkinson's Disease Rating Scale (UPDRS) (on-stim, off-stim, on-med, off-med), PDQ-39, MMSE, ADL score. Patients with dystonia were evaluated with Burke-Fahn-Marsden-Dystonia (BFMDRS) or Toronto-Western-Spasmodic-Torticollis (TWSTR) rating scale.

RESULTS: In the off-medication state, STN stimulation improved the mean UPDRS part III score by 54%. The levodopa equivalent daily dose for patients with PD decreased on 38%. The improvement of motor signs of PD to STN stimulation was strongly positively correlated with responsiveness to levodopa test. The average improvement of dystonia symptoms after bilateral GPi stimulation was 62% (from 31 to 72 %). There were no serious neurological complications. One patient with GPi stimulation has had moderate persistent photopsia, which didn't affect his daily activity.

CONCLUSION: Stimulation of STN and GPi significantly improves many features of PD and dystonia and can be safely used in carefully evaluated patients with few side effects.

PAIN I

ORAL PRESENTATIONS

1/OR20

GAMMA KNIFE RADIOSURGERY FOR GLOSSOPHARYNGEAL NEURALGIA: REPORT OF 7 CASES

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Introduction

Although Gamma Knife radiosurgery (GKR) is widely recognized as an effective and minimally invasive treatment for intractable trigeminal neuralgia, its role in glossopharyngeal neuralgia (GPN) has not yet been determined.

Methods

Between January 2002 and February 2009, 7 patients with medically intractable GPN were treated using GKR. Indication for GKR was the presence of medically intractable GPN and patient's refusal or contraindication to microvascular decompression. Patients underwent preoperative investigation and were evaluated postoperatively with periodic assessment of pain relief and neurological function.

Results

Seven patients (5 male, 2 female, mean age 64, range 49-83) presented with symptoms for an average of 28 months (8-72). Four patients had a vasculo-nervous conflict. Patients were treated with a dose ranging from 60 to 80 Gy, targeted on the cisternal segment (n=2) or GlossoPharyngeal Meatus (GPM) (n=5). Outcome was favorable with cure of GPN in 5 of 7 patients (71%) in the short-term (3 months) and 4 of 7 (57%) patients in the long term (16 months). One patient required 2 treatments because of a recurrence of symptoms and was treated with a maximum doses of 60 and 70 Gy, respectively. There were no neurological complications.

Conclusion

All patients with GPM as a target that received a dose greater than 75 Gy were cured at long-term follow-up. The 2 patients with cisternal segment as the target and received a dose significantly lower than 70 Gy were not cured of their GPN. There were no neurological deficits involving the lower cranial nerves. It will be necessary to investigate the optimal radiation dose and target of GKR for GPN in order to achieve long-term pain relief.

2/OR21

DEEP BRAIN STIMULATION FOR DRUG-REFRACTORY CHRONIC CLUSTER HEADACHE A LONG TERM EVALUATION OF SAFETY AND EFFICACY

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OBJECTIVES :

To assess long-term effects following continuous hypothalamic stimulation in 5 intractable patients with chronic Cluster Headache (CH).

METHODS :

After approval of Ethics Committee, patients were selected according to ICDH-II criteria and drug failure was verified. Patients underwent image-guided (3DT1 MRI) stereotactic implantation of a quadripolar electrode into the ipsilateral posterior hypothalamus.

Patients were evaluated on : number and intensity of attacks/week, number of subcutaneous sumatriptan injection / week, quality of life (SF12) and adverse effects.

Long-term neuroimaging (intra-op MRI and CT Scan fusion) verify the actual coordinate of active contact.

RESULTS :

At a mean follow-up of 4,5 years (47-64 months), all the patients are responders (more than 50 % decrease in weekly attacks frequency and need for rescue drugs).

Only one patient is persistently pain -free (during the last 2 years and the 4 others have observed a progressive and also late efficacy . All the patients report a significant improvement in quality of life. At long-term, there are no side-effects

For 3 patients the active is still the deepest (0-), and (1-) for the 2 others.

There is no complication on the electrode trajectories and no displacement in follow-up CT control imaging ; Mean position of active contact relative to the AC_PC landmarks was 3,5 mm (range 1 ,5 to 4,7) behind the midcommisural point , 5,2 mm (range 4,6 to 6) below this point , and 2,6 mm (0,4 to 5) lateral from midline . These coordinates were very close to theoretical target used in this study and published by Franzini and al. There is no consensus as to whether this anatomical area is part of the posterior hypothalamus or the anterior periventricular grey matter .

CONCLUSION :

Chronic deep brain stimulation (DBS) in hypothalamic area is well-tolerated and effective. Intractable and drug-resistant chronic C.H has evolved into a tolerable episodic form.

SUBCUTANEOUS OCCIPITAL NERVE STIMULATION FOR THE TREATMENT OF DIFFERENT HEADACHE SYNDROMES

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Objective:

Medical treatment for different headache syndromes can be challenging and hindered by intolerable side effects. Since several years occipital nerve stimulation is considered to be a neuromodulative procedure to ameliorate certain headaches as chronic migraine, hemicrania continua, chronic cluster headache and others. However the operative technique has changed. The electrodes are not placed anymore in the nearest vicinity of the greater occipital nerve but subcutaneously. This report summarizes the experience of ten patients with unilateral or bilateral subcutaneous occipital stimulation in different headache syndromes.

Methods:

Since 2005 10 patients with different headache syndromes were operated on with uni- or bilateral subcutaneous occipital stimulation. All patients were treated by conservative measures as medication of at least 12 months, 5 of ten underwent diagnostic blocks. In 7 patients a unilateral lead electrode were implanted, in 3 bilateral electrodes. In one patient the electrodes were explanted and bilateral plate electrodes were used due to the high energy consumption.

Results:

Of the ten patients 4 suffered from chronic cluster headache (CCH), 2 from chronic migraine (CCH/CM), one from mixed pain (CCH+CM) and three from typical occipital neuralgia (ON). Follow-up ranged from 6-54 months (mean 22.1 months). All patients experienced major pain relief at the last follow-up with improvement from 70-100%. Best results were yielded in ON. In CCH and CM the frequency and intensity of the attacks were significantly reduced but not abolished. Medication could be reduced markedly in all patients.

Conclusion:

Subcutaneous occipital stimulation is a minor invasive procedure and leads to similar results, especially in CCH as compared to DBS. It seems to be a meaningful adjunct to medical treatment in so called intractable headache syndromes.

4/OR23

SPHENOPALATINE GANGLION (SPG) STIMULATION TO TREAT ACUTE MIGRAINE AND CLUSTER HEADACHES

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Objectives: The sphenopalatine ganglia (SPG) is a parasympathetic and sympathetic ganglia that is implicated in the pathophysiology of cluster and migraine headaches. SPG blocks and Lesioning have been used for years with safety and efficacy for these disorders. We performed a study of SPG stimulation for acute treatment of migraine and cluster headaches.

Methods: After research committee approval (IRB), severe and refractory migraine and cluster patients underwent fluoroscopic guided percutaneous temporary neurostimulation electrode placement. The headaches were present spontaneously or were triggered to a maximal headache intensity. SPG stimulation was then initiated while monitoring pain (VAS), vital signs, autonomic changes, and neurological status.

Results:

Cluster Headaches - Five patients underwent a total of eight acute stimulation trials resulting in 19 distinct acute cluster headaches of clinically maximal intensity (VAS > 8). 11/18 acute headaches resolved completely with SPG stimulation, 3 were partially improved (> 50% VAS reduction) and 5 had minimal to no relief.

Migraine Headaches - Ten patients underwent 10 acute stimulation trials. SPG stimulation resulted in 2 patients with complete headache resolution, 2 with partial relief (> 50% VAS reduction) and 6 with minimal (<50% VAS reduction) or no relief. Both cluster and migraine patients had improvements in the associated nasal congestion and periorbital edema improved. The headache improvements occurred acutely within 5 minutes of stimulation. There were no complications except for one case of transient epistaxis.

Conclusions: This study suggests a potential role for SPG stimulation for treating acute cluster and migraine headaches. SPG stimulation appears to be modulating the circuitry involving cluster and migraine headaches.

5/OR24

PERIPHERAL SUBCUTANEOUS NERVE STIMULATION

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Introduction

After the introduction of stimulation techniques for the treatment of chronic pain by means of SCS and PNS in the 70s, PNS-stimulation for treating Mononeuropathy, as well as sympathetic pain (Weinert 2003), underwent a renaissance. PNS techniques were introduced for treatment of CRPS I (Hassenbusch 1996), occipital neuralgia (Oh and Withing 1999), migraine (Popney and Alo 2003), as well as neuropathies (Eisenberg 2004).

Patients and Methods

Following the convincing results, introduced by Barolat 2004, we performed a so called "Field Nerve Stimulation" pilot study from May 2005 to February 2006.

Indication was a well described exactly localized area of pain, partly connected to Allodynia. After the exclusion of radicular pain, this method was considered the first step of invasive pain therapy on the neurosurgical pain scale (Tab.1), which was independent of medication. Twelve patients suffered of lumbar pain syndrome, three of occipital neuralgia, three of knee pain, three of root avulsion, one of post-thoracotomy syndrome, four of neuropathic facial pain, two of phantom pain, two of CRPS I, as well as one pain syndrome after inguinal hernia. The patients were assessed, both post-operatively and after a Follow-Up period of one year, using the VAS scale. Leads were placed, allowing accessing the outer border of the area of pain (Fig. 1, 2, 3, 4, 5, and 6).

After a one-week trial-phase, the trial electrodes were removed and replaced by permanent subcutaneous electrodes in the same location, which were later on connected to a completely programmable generator. Eleven out of thirty-one Patients (Tab.2), who received an implantation of one to four leads (quadrode/octrode) and then underwent a one-week trial-phase, received an implantation of a complete system.

Discussion

Approximately 30% of the patients displayed a pain relief of more than 50% for a period of up to one year. 16 patients (Tab.3), who did not profit from peripheral nerve stimulation, were treated by SCS, according to our therapy scale. Since an adequate pain relief could not be achieved by SCS either, it can be assumed that simple subcutaneous stimulation can serve as a predictor for the success of spinal stimulation. In addition, patients who subsequently received an intrathecal opiate therapy showed significantly weaker results than other patients.

Conclusion

Peripheral nerve stimulation is a simple, promising method, with the best indication being a well localizable pain, and can be considered as the first step of invasive pain therapy for treating well described pain emission. The operation technique is very simple and of low risk, however, long term results have to be awaited.

ORAL POSTERS

1/OP16

DEEP BRAIN STIMULATION OF THE PERIAQUEDUCTAL GREY AREA IN CHRONIC PAIN: A TARGET STRUCTURAL AND CONNECTIVITY STUDY

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Introduction

Deep Brain Stimulation (DBS) of the periaqueductal/periventricular grey area (PAG) has been an effective treatment for certain types of chronic pain. Neuroimaging abnormalities of this area have been demonstrated in chronic pain. We analysed neuroimaging abnormalities and connectivity of the PAG in a cohort of PAG DBS patients with chronic pain.

Methods

Patients (n=15) who subsequently were treated with PAG DBS and healthy control subjects were enrolled for neuroimaging data acquisition. Diffusion tensor imaging data was acquired using echo planar imaging. After correction of eddy current distortion, FA images were generated by fitting a tensor model to the diffusion data. Stereotactically aligned FA data was passed into voxelwise cross-subject statistics, using a permutation-based inference tool for nonparametric statistical thresholding. Bayesian estimation of diffusion parameters was then performed, using Markov Chain Monte Carlo sampling. Probabilistic tractography was performed of the PAG. Structural imaging data was analysed using a voxel-based morphometry style analysis. Segmented, aligned data was modulated and smoothed with a Gaussian kernel. Voxelwise general linear model statistics was applied using permutation-based non-parametric testing.

Results

Voxelwise analysis of FA demonstrated increased FA of the PAG in chronic pain ($p < 0.001$). Voxel based morphometry analysis of structural data demonstrated reduced grey matter density of the PAG/PVG ($p < 0.001$). The connectivity profile was reduced in chronic pain patients, including reduced connectivity with the orbitofrontal cortex in chronic pain. Topographic mapping of each voxel's connectivity with cortical regions demonstrated altered topography in chronic pain. Patients with successful outcome from PAG DBS demonstrated different connectivity profiles compared with unsuccessful response to DBS, including increased connectivity with the brainstem.

Conclusion

Altered connectivity of the PAG with known pain pathways in the chronic pain state, increases our understanding in the role of the PAG in pain and may help explain the effectiveness of DBS of this target. This analysis may be applied to help predict patient response to PAG DBS and preoperative characterization of PAG functional connectivity may help in patient selection. It may be useful to characterize PAG connectivity to customize surgical targeting and help determine the optimal site for electrode insertion.

2/OP17

BIFOCAL CORTICAL ELECTRICAL STIMULATION FOR PAIN BY INTERDURAL IMPLANTATION OF THE ELECTRODES

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Objective: To evaluate the efficacy of unifocal or bifocal electrical cortical stimulation (ECS) in the alleviation of medically-refractory pain by interdural implantation of the electrodes.

Method:

A modified technique, *interdural* ECS that involves resection of a strip of dura and "patch-like" placement of the electrodes over the motor and the sensory cortices, was applied in five patients with treatment-refractory pain syndromes: a 76-year old female with post-stroke central pain, a 71- and a 73-year old female with trigeminal neuropathic pain, a 44-year old male with phantom limb pain and a 32-year old male with neuropathic pain after brachial plexus avulsion.

In all patients, we offered ECS according to predetermined protocol: a) single motor, b) single sensory and c) combined (i.e. bifocal) motor/sensory stimulation, with the electrode over the motor cortex functioning as the cathode (negative contact) and the electrode over the sensory cortex functioning as the anode (positive contact).

Results:

In all patients, during programming sessions, impedance values remained constant within a narrow range. Single motor ECS offered improvement ranging from 45-60% in pain intensity, single sensory ECS improvement ranging from 20-30% and combined, i.e. bifocal, motor/sensory ECS improvement ranging from 65-90%. The highest possible benefits resulted from combined stimulation of the motor/sensory cortices. All five patients have experienced a significant improvement in their quality of living. The follow-up ranges from 6-30 months.

Conclusions:

Bifocal interdural ECS holds the promise to improve the efficacy and consistency of ECS compared to the standard epidural or subdural ECS without increasing the risk of the procedure. The technical considerations and the potential therapeutic advantages of the interdural approach are discussed.

3/OP18

HOW SAFE IS IT TO REPEAT PERCUTANEOUS GLYCEROL RHIZOTOMY FOR TRIGEMINAL NEURALGIA?

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Objective:

Percutaneous glycerol rhizotomy (PGR) is an established surgical treatment option for trigeminal neuralgia. Our aim was to establish how safe repeat injections were to the patient.

Methods:

A retrospective study on 179 percutaneous glycerol rhizotomies performed in our institution.

Results:

An overall success rate in subjective improvement in facial pain was seen in 92.1%. The mean time to repeat injection was 22.9months. Complications of glycerol rhizotomy included difficulty in finding foramen ovale (5), abandoned due to bleeding (3), asystole on needle insertion (1), reduced facial sensation (9). There was no significant increase in complications with repeat PGR, with patients having up to six procedures. There were no episodes of anaesthesia dolorosa.

Conclusion:

Percutaneous glycerol rhizotomy for trigeminal neuralgia is safe, effective and repeatable.

4/OP19

Motor Cortex Stimulation – is important method in the complex treatment of central neuropathic pain.

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Objectives: to evaluate the efficacy of MCS for patients with central neuropathic pain (NP).

Methods: 12 patients (5male, 7 female, mean age 40,8) with severe NP underwent MCS: 1 case - multiple sclerosis (MS) and anesthesia dolorosa (AD); 4 - NP after traumatic noncomplete preganglionic lesion of a brachial plexus; 1 – NP after removal of neurinoma at level C6-Th1 and subsequent DREZ-operation; 1 - NP in arms, legs and trunk (below Th3) after the cerebrospinal injury (C6), 3 – Poststroke pain and 2 – Phantom limb pain (in phantom arm). Frameless neuronavigation technique with intraoperative electrophysiological control was applied for implantation of two "Resume"-electrodes on the central cortex. In 10 cases we use "Synergy" IPG, and in two cases – "Kinetra" system. NP was assessed by VAS and verbal-color test.

Results:In the early period and in follow-up (30 months) good results have been received in all cases. Intensity of pain in comparison has decreased more than on 50 %. Parameters of MCS: 1,0-5,5 V, 20-50 Hz, 60-210 μ s. All patients have stopped narcotic analgesics.

Conclusions: MCS is important method of treatment severe NP. Efficiency of treatment related of the psychogenic component of complex pain syndrome and of expressiveness deafferentation symptoms. In cases with low-grade density of these factors results are better and longer.

IMPLANTATION OF PLATE ELECTRODES FOR SCS UNDER SPINAL ANESTHESIA AND MINI-INVASIVE LAMINOTOMIC APPROACH.

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Aims: the implantation of plate electrodes for spinal cord stimulation (SCS) is often performed under local anesthesia, allowing the best positioning and minimizing the risk of further re-positioning. However, this procedure involves serious discomfort and pain for the patients. Thus, we experienced the implantation under spinal anaesthesia in order to obtain the finest positioning of the plate, avoiding pain sensation and minimizing the patients' discomfort.

Methods: 16 patients (14 FBSS; 1 multiple sclerosis, 1 luetic arachnoiditis) underwent the implant of plate electrodes for SCS in lateral position. Spinal anesthesia was induced by 12.5-20 mg of Bupivacaina. Further local infiltration (Mepivacaina 2%) around the incision was performed. After removal of interspinous ligament and flavectomy we introduced the plate electrodes and the stimulation test started. The patients were asked to confirm the paresthesias' coverage in the painful dermatomers.

Results: all patients were implanted without discomfort. In all the cases the complete paresthesias coverage of the painful region was achieved with 1.2-2 V intensity, allowing the finest definitive positioning, despite the spinal anesthesia. At the last follow-up (mean value 32,5 months) the VAS score improvement was more than 50% in 14 patients. No re-repositioning was needed.

Conclusions: the implantation of plate electrode under spinal anesthesia is a safe technique, enabling an intraoperative on-line evaluation of the paresthesias coverage and allowing the optimal plate positioning without discomfort. The finest final positioning of the plate is confirmed by the improvement of VAS score in most of the patients and by the absence of repositioning.

6/OP21

CARDIOVASCULAR RESPONSE DURING TRIGEMINAL GANGLION COMPRESSION FOR TRIGEMINAL NEURALGIA ACCORDING TO THE USE OF LOCAL ANESTHETICS

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Objectives: There are controversies about using local anesthetics during balloon compression for trigeminal neuralgia as a protective factor for cardiovascular events. The objective of this study was to investigate cardiovascular parameters (blood pressure and heart rate) during trigeminal balloon compression with local anesthetics and to compare to a control group.

Methods: Case-control study; 55 patients were referred for trigeminal ganglion compression and randomized in 2 groups: Study Group (deep sedation and local anesthetics) and Control Group (deep sedation only). Blood pressure and heart rate were measured during all the procedure. After data collection, statistical analysis was performed with analysis of variance for repetitive measures and nonparametric McNemar test.

Results: It was observed statistically lower increase of heart rate and blood pressure in the Study Group when compared to the Control Group ($p=0.018$).

Conclusion: the use of local anesthetics had a preventive role for the cardiovascular risk during balloon compression of the trigeminal ganglion for trigeminal neuralgia.

Keywords: trigeminal neuralgia, general anesthesia, local anesthetics, trigeminal block, facial pain, functional neurosurgery, balloon compression.

EPILEPSY

ORAL PRESENTATIONS

1/OR25

ADVANCES IN THE SURGICAL TECHNIQUE FOR STEREOELECTROENCEPHALOGRAPHY (SEEG) IN EPILEPSY SURGERY: A RETROSPECTIVE ANALYSIS OF GEOMETRICAL ACCURACY AND SAFETY FOR THE IMPLANTATION OF 282 INTRACEREBRAL ELECTRODES

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Introduction

In the period of May 1996 – April 2010 we performed 438 SEEG procedures in 412 patients, implanting 5692 intracerebral electrodes. The original Talairach methodology was progressively integrated with new tools (MRI, stereotactic planning software, robotics), especially in the last year (3D angiography, 3D brain surface reconstructions). Major intracranial bleedings occurred in 4/438 procedures (4/5692 trajectories - 0.07%). One three years old child died of massive global brain oedema, probably due to severe hyponatremia.

Objectives

The objective of this study was to analyze retrospectively geometrical accuracy and safety of a new methodology for SEEG electrode implantation.

Methods and subjects

In the period of September 2009 – April 2010 we performed the last 23 SEEG procedures, implanting 282 intracerebral electrodes. Every patient received preoperatively 3D MRI and 3D brain angiography acquired with the O-arm™ 1000 System (Medtronic), without any frame. All the images were post-processed with a custom-made automatic procedure (based on open-source software tools) before importing them into the stereotactic planning software. All the electrodes were implanted with the aid of the stereotactic image guided robotic system Neuromate® (Renishaw mayfield). The euclidean distance between the plan and the real position of the implanted electrodes at the entry point was measured.

Results and conclusions

The mean euclidean distance at the entry point was 0.88 mm (\pm 0.56). The brain targets were reached for all trajectories. There were no major complications in the 23 procedures performed with the new methodology. These data suggest that the new methodology is highly accurate and safe.

2/OR26

SCALP AND DEEP EEG IN DBS FOR EPILEPSY

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The treatment of pharmacoresistant epilepsy with deep brain stimulation (DBS) gained interest in last years and literature data showed good results after bilateral stimulation of centromedian thalamic nucleus (CM) in Lennox-Gastaut syndrome (LGS). The efficacy of the bilateral stimulation of CM could be related to the inhibition of seizure propagation in patients with generalized seizures, whose focal onset is not defined.

We describe scalp and deep EEGs, recorded from implanted bilateral thalamic electrodes, in three patients, who underwent DBS of CM for refractory epilepsy.

One patient is an eleven years old boy with typical LGS, the other two are adults with symptomatic (dysplastic) or cryptogenic Lennox like epilepsy. We recorded all three patients in operating room, after neuroleptoanalgesia, with scalp electrodes positioned according to the International 10-20 System. The boy was recorded also from deep electrodes. The day after surgery, the adult patients were recorded for 24 hours (from scalp and depth electrodes), during wakefulness and sleep.

Preoperative EEGs showed diffuse ictal and interictal discharges of spikes and spike and waves. During intraoperative recordings we observed a loss of synchronism of epileptiform scalp abnormalities.

At visual analysis, interictal and ictal epileptiform recorded from deep and scalp recordings appeared synchronous between cortex and thalamus. This finding (that we will further evaluate by appropriate methods of EEG analysis) would suggest a remarkable participation of CM nucleus in seizure generation.

A correlation between epileptiform thalamic activity and good outcome could give a prognostic significance to such EEG activity.

3/OR27

DEFINITION OF A STEREOTACTIC 3D MODEL OF THE HUMAN INSULA FOR NEUROSURGICAL APPROACH (EPILEPSY AND STEREOTAXIC SURGERY)

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Objectives

Design a method for 3D reconstruction of the insula, including its gyri and sulci , in AC-PC reference usable individually for imaging or for epilepsy and stereotactic surgery.

Materials - Methods

Morphometric study using 56 MRI of normal insular region. 26 male/30 female, 28 left/28 right hemispheres.

Stage 1 : Reconstruction in AC-PC reference of the insula from 3D-T1-MRI slices 1 mm thick.
Stage 2 : Digitalization and superposition of data in 3D using PhotoStudio software (Photo Editing Software) system with PC as the center of coordinates.

Stage 3 : MATLAB software (Mathworks Inc.) was used to transform in color values each pixel to obtain a color scale corresponding to the probability of insula sulci localization between 0% and 100%.

Results

Demonstration of very significant correlations between the coordinates of the main insular structures (angles, sulci ..) and the length of AC-PC.

This close correlation allows to describe a method for 3D reconstruction of the insula on MRI slices that requires only the positions of Ac and PC and then the inter-commissural (AC-PC) length. This procedure defines an area containing insula with 100% probability.

Conclusion

3D reconstruction of insula will be potentially useful for:

- 1- To improve localization of cortical areas, allowing to differentiate insular cortex from opercular cortex during stereoelectroencephalographic exploration of patients with epilepsy (SEEG) or in morphological and functional imaging.
- 2 - For microsurgical approach of Insula using Neuronavigation techniques.
- 3 - Identification of Insula during stereotactic surgery (SEEG, biopsy).

4/OR28

**AMYGDALOHIPPOCAMPOTOMY:
SURGICAL TECHNIQUE AND RESULTS IN 20 CASES**

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Background: Removal of epileptogenic foci involving temporo-mesial structures by amygdalohippocampectomy is the most efficient surgical procedure for treatment of epilepsy. However, disconnection instead of removal of large epileptogenic zones, like hemispherotomy or temporal lobotomy, has shown equivalent results with less morbidity. Since 2007 we performed selective amygdalohippocampotomy in all cases of refractory temporo-mesial epilepsy for temporo-mesial lobe sclerosis (TLS).

Method: Twenty patients (13 females) aged 20-58 years (mean: 41y) were operated with this technique: selective ablation of lateral amygdala plus peri-hippocampal disconnection (2/3 anterior on dominant hemisphere); left side on 11 cases, right on 9. Follow-up time: 2- 30 months (average: 15 months).

Results: One patient was excluded because an extra-temporal lesion and focus were also diagnosed. Operative time was reduced with this technique by 30 minutes (15 %) in average. Histopathological diagnosis: TLS with amygdala gliosis in 18 patients (in one patient material wasn't enough). Surgical outcome: good/very good in all 19 patient, with Engel Class I-A in 16 (84,2%), II-A in 2 (10,5%) and II-B in 1 (5,3%). Surgical morbidity: one patient with hemiparesis (hypertensive haemorrhage 12 hours after surgery), 2 with memory worsening, 1 with quadrantanopia; 2 cases of late transient psychiatric depression.

Conclusions: Amygdalohippocampotomy is as effective and safe as amygdalohippocampectomy, has less intraoperative risks and is slightly time-saving. The surgical technique is video-illustrated during the presentation.

5/OR29

TRANSCORTICAL T2 SELECTIVE AMYGDALOHIPPOCAMPECTOMY FOR THE TREATMENT OF DRUG RESISTANT MESIAL TEMPORAL LOBE EPILEPSY WITH THE USE OF A NEW SELF-RETAINING BRAIN RETRACTOR.

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Purpose: Although Anterior Temporal Lobectomy remains the most frequently performed operation, for intractable mesial Temporal Lobe Epilepsy, the trend nowadays is towards more selective approaches and resections. The purpose of this study is to assess the seizure outcome, comparing it with data from the literature, and to underline the significance of a specific self-retaining brain retractor.

Methods-Materials: Thirty consecutive patients were selected among a series of 42 patients who were treated surgically for MTLE, by means of transcortical selective amygdalohippocampectomy. The remaining 12 were treated with Anterior Temporal lobectomy and amygdalohippocampectomy. An eye – lid retractor was transformed into a self retaining brain retractor with blades 2.5 X 3cm replacing the Leyla retractors.

Results: The follow-up period in this series was up to 9 years with 72% of patients in Engels Class I and 16% in Engels class II. None of them had any significant visual field deficit.

Conclusions: The results of the transcortical T2 selective amygdalohippocampectomy, regarding the clinical outcome and the complication rate, were at least as good as those reported in literature. This type of approach using the specially designed self retaining retractor is effective and safe with minimal cortical trauma and without the hazards of splitting the Sylvian fissure as in the transylvian amygdalohippocampectomy.

6/OR30

CORTICAL MICRO-TRANSECTIONS BY SYNCHROTRON-GENERATED MICROBEAMS INDUCE NEUROMODULATION OF SEIZURES SPREADING PATTERN IN AN ANIMAL MODEL OF EPILEPSY: PRELIMINARY RESULTS.

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Objectives: cortical transections (CT) have is a surgical approach to treat drug resistant epilepsy with epileptic foci located in eloquent cortex. Synchrotron-generated microbeams have been tested to produce CT in the motor cortex (MC) of a kainic acid (KA) rat model of focal epilepsy.

Methods: we have analyzed the ability of microbeams to transect left MC without inducing deficits. An array of 7 microbeams in 12 rats and 4 different microbeam size (25, 60, 100 and 600 μ .m) were tested. We analyzed than the ability of microbeam transections to stop seizures induced by KA injection over the left MC with 100 μ .m and 600 μ .m beams in 6 rats. Two subgroups of 3 animals received high-dose (360 Gy for 100 μ .m and 150 Gy for 600 μ .m) and low-dose (240 Gy for 100 μ .m and 100 Gy for 600 μ .m). Twelve rats receiving only KA injections were used as controls.

Results: after 9 months of follow-up rats no sign of neurological deficits developed in healthy animals. Immunohistochemical analysis confirmed the presence of the lesion. KA injection into the left motor cortex induced severe seizures. Seizures duration was reduced in the rats with transections and no dead were recorded. with high ad low dose. A similar results was obtained in the 600 μ .m beams group at 130 and 160 minutes.

Conclusion: this preliminary results demonstrate the feasibility of synchrotron-generated CT in the modulation of cortical seizure spreading. This irradiation technique for eloquent cortex can induces fast relief of seizures without any damage of neurological functions.

BITEMPORAL EPILEPSY- COULD IT BE SURGICALLY TREATABLE?

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Objective.

The purpose of this study is to achieve beneficial treatment outcomes for severe intractable bitemporal epilepsy patients, who, in most cases are not considered as optimal candidates for resective epilepsy surgery using neurophysiologically guided stereotactic surgery.

Methods.

Twenty-one intractable epilepsy patients (13 men, 8 women,,6-43 years of age, mean 3-31 years of duration of illness, frequency of seizures 6 to 55/mo) underwent multitarget stereotactic cryosurgery including bilateral hippocampal formation elements guided by pre- and intraoperative depth electrode evaluation.

Results.

The SEEG studies revealed the existence of complexly organized multistructural epileptic systems involving mesio-basal structures of both temporal lobes in cases of long-standing severe intractable epilepsy. Engel's (1993) Class I outcome was achieved in 51%, worthwhile improvement (Classes II-III) was observed in 28% and no worthwhile improvement (Class IV) was observed in 21% of all patients. Remarkable normalization of the psycho-emotional state was achieved for patients with presurgical behavioral problems. No seizure, or cognitive, or memory states worsening was observed in this cohort of patients. The follow-up for seizures and behavioral abnormalities was up to 10 years.

Conclusion.

Electrophysiologically guided stereotactic surgery can have a beneficial effect on seizure frequency and severity, psycho-emotional state, and behavior in long-standing intractable bitemporal epilepsy patients, and existing thesis about the contraindications for bitemporal epilepsy surgery should be reconsidered. The carefully planned multitarget stereotactic surgery does not necessarily lead to a postsurgical decline in intelligence, learning, and especially memory, and the benefits of seizure control outweigh the risk of further cognitive decline.

8/OR32

**SURGICAL TREATMENT OF CORTICAL DYSGENESIA - ASSOCIATED EPILEPSIES
IN ADULTS**

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Keywords: epilepsy, focal cortical dysplasia, topectomy, gray matter heterotopia, focal pachygyria

Objectives: to analyse the morphological findings and results of surgical treatment of adult patients with cortical dysgenesis – associated epilepsies.

Materials and methods: 12 patients with various cortical dysgenesias were operated. The topectomy was done in all cases after pre-surgical evaluation which obligatory included an MRI – scan (T1, T2, FLAIR axial, sagittal and coronal series), fMRI with navigation, EEG – video and invasive corticography for every patient.

Results: The mean age of patients was 26 years (between 17 and 33 years). The mean duration of disease was 9.7 years. There were 7 females and 5 males. The MRI scan showed FCD in 7 patients, focal pachygyria in one patient and gray matter heterotopia in one patient. Three patients haven't had any visible abnormalities on MRI. All patients underwent an invasive corticography before the surgical resection to identify the epileptogenic region which was resected afterwards using the intra-operative navigation and corticography before and after topectomy. In five cases awake-craniotomy was performed for patient with dysgenesis located in eloquent brain areas. There was no neurological complication. The morphological examination confirmed FCD I type in 4 cases, FCD IIa in 3 patients and IIb –in 3 patients, focal pachygyria in one case and gray matter heterotopia in one case. The three-years follow – up showed a complete seizure-free outcome in 6 patients (Engel Ia), 5 patients achieved Engel II (rare partial seizures) and one patient has Engel III outcome.

Conclusion: dysgenesis – associated pharmaco-resistant epilepsies in adult patients can be successfully treated with topectomy without neurological complication.

ORAL POSTERS

1/OP22

ARE SUBCLINICAL ABNORMAL GYRATION PATTERN, ANATOMICAL MARKER OF EPILEPTOGENIC ZONE IN PATIENTS WITH MRI-NEGATIVE FRONTAL LOBE EPILEPSY ?

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Background: Epilepsy surgery for MRI-negative patients has a less favorable outcome. Objective: Detection of subclinical abnormal gyration (SAG) patterns and its potential contribution to assessment of the topography of the epileptogenic zone (EZ) is addressed in MRI-negative frontal lobe epilepsy (FLE) patients. Methods: Between September 1998 and July 2005, 12 MRI-negative FLE patients underwent stereoelectroencephalography (SEEG) with post-cortectomy follow-up of longer than 1 year (average 3.3 years). Original software (BrainVISA/Anatomist, <http://brainvisa.info>) trained on a database of normal volunteers was used to determine which sulci had morphology statistically out of the normal range (SAG). Topography of the EZ, SAG pattern, cortectomy, post-operative seizure control and histopathology were analyzed. Results: At last follow-up, 8/12 patients (66.7%) were Engel class I (7 IA), 2 class II, and 2 class IV. Small focal cortical dysplasia (FCD) was histologically diagnosed in 9 (75%) of the 12 patients, including 7/8 seizure-free patients (87.5%). SAG pattern was found to be within the EZ area in the ipsilateral frontal lobe in 9 patients (75%), out of the EZ in 2 and limited to the contralateral hemisphere in 2. Conclusion: SAG patterns appear to be significantly associated with the topography of the EZ in MRI-negative FLE and may have a useful role in pre-operative assessment. Small FCD not detected with MRI are often found at histopathological examination, particularly in the depth of the posterior part of the superior frontal sulcus and intermediate frontal sulcus, suggesting a specific developmental critical zone in these locations.

CONNECTIVITY OF THE ANTERIOR NUCLEUS OF THALAMUS IN EPILEPSY

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Introduction

Deep Brain Stimulation (DBS) of the anterior thalamic nucleus (ATN) is currently under clinical investigation for refractory epilepsy. Using diffusion tensor imaging techniques it is possible to determine connectivity patterns of neuronal tissue. We characterized the functional connectivity profile of the ATN in refractory frontal and temporal lobe epilepsy and control subjects using diffusion tensor imaging based probabilistic tractography and topographic mapping to determine neuroimaging evidence for potential DBS applications.

Methods

Diffusion weighted data was acquired using echo planar imaging in 8 patients with refractory frontal or temporal lobe epilepsy and healthy control subjects. After correction of eddy current distortion, fitting of diffusion tensors, Bayesian estimation of diffusion parameters using Markov Chain Monte Carlo sampling was carried out. Probabilistic tractography was performed to characterize connectivity profiles of the ATN. Topographic mapping of ATN connectivity with predefined cortical targets areas was used compute changes in dominant cortical connectivity patterns.

Results

In temporal lobe refractory epilepsy a reduction in ATN connectivity was demonstrated, notably less connectivity across the corpus callosum with the contralateral hemisphere ($p < 0.05$) and the cingulum. A similar connectivity profile was demonstrated in frontal lobe epilepsy although contralateral connectivity across the corpus callosum was higher than in temporal lobe epilepsy. Topographic mapping demonstrated alterations in dominant target connectivity patterns of the ATN in epilepsy compared with controls.

Conclusion

This study demonstrates altered ATN connectivity in refractory epilepsy. The temporal lobe epilepsy ATN connectivity profile demonstrated more significant abnormalities than frontal lobe epilepsy. These techniques may provide useful information to aid in patient selection and surgical targeting in ATN DBS for epilepsy.

LOCALIZING SIGNIFICANCE OF EPIGASTRIC AURAS: RESULTS OF INTRACRANIAL STIMULATION STUDY

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Introduction: Previous electrophysiological studies have identified the mesial temporal structures as the most common sites of epigastric auras in cases of mesial temporal epilepsy. However, the possibility that epigastric auras may also originate from limbic sites other than mesial temporal structures has been postulated. The purpose of our current retrospective study was to assess the occurrence of epigastric auras in cases of electrical stimulation, and identify the anatomical site of their origin.

Material & Methods: The data of electrical stimulation studies of 50 consecutive patients undergoing invasive electro-encephalographic recording for preoperative evaluation of medically intractable epilepsy were collected and were analyzed. A Grass 88 or 12 stimulator was used for delivering balanced, biphasic square-wave pulses of 0.5 msec pulses, of 0.5-12 mA intensity, and 3 sec train duration. Post-implant skull x-rays were routinely obtained and the implanted electrode contacts were localized by employing the Talairach-Tournoux atlas on the obtained x-rays.

Results: A total of 98 analyzable responses were obtained from 28 patients. There were 68 depth and 30 subdural electrode responses. There were 17 responses regarding viscer-autonomic functions, and 9 of these were expressed as epigastric sensation responses. Eight of these epigastric responses were elicited from the left and only one from the right hemisphere. More specifically, three originated from the mesial frontal area, one from the orbito-frontal, three from the insulo-opercular area, and two from the mesio-basal temporal area.

Conclusions: Although the majority of epigastric responses to electrical stimulation originated from the mesial temporal structures, insular areas were also involved in their development. Our findings suggest that other limbic structures may be implicated in the pathogenesis of epigastric auras.

MIDDLE SHORT GYRUS OF THE INSULA IMPLICATED IN SPEECH PRODUCTION: INTRACEREBRAL ELECTRIC STIMULATION OF PATIENTS WITH EPILEPSY

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Objectives

Few data exist about the role of the insula in the processing of speech. The data of this study suggests the involvement of the upper middle short gyrus in speech production.

Materials-Methods

For this study, we included 25 patients suffering from severe drug refractory partial epilepsy were investigated by stereo-electroencephalography (SEEG). At least one electrode was used to explore the insular cortex using an oblique approach (trans-frontal or trans-parietal) and who had a normal insular region. 313 stimulations were performed in 27 insula. 83 responses induced by insular electrical stimulation (ES), eight (9.6%) were reported by five patients as speech arrest (5 responses) and a lowering of voice intensity (3 responses). The stereotactic approach allows us to identify the stimulation sites within the insular cortex in terms of its gyri and sulci. Also, the stimulation sites were anatomically localized via image fusion between pre-implantation 3D MRI and post-implantation 3D CT scans revealing the electrode contacts.

Results

8 responses were reported as speech disturbances. 7 among them were evoked in 4 patients by stimulation in the middle short gyrus (8.4% of total responses, and 25.9% of responses evoked in the middle short gyrus). The site of the 8th response was in the post-central insular gyrus in the same insular region where the oropharyngeal responses induced by other ES (pharyngeal constriction) in this study.

The data suggest the involvement of the middle short gyrus of the insula in the procedures of language. These responses were evoked in the non-dominant side four times out of five. This study provides evidence that the middle short gyrus of the insula in both hemispheres responds to ES producing speech disturbances.

Conclusion

The results of this study are the first to report language disorders in humans evoked by electrical stimulation of the insular cortex during SEEG explorations by electrodes implanted by oblique approach in terms of gyral and sulcal anatomy.

CYTOKINE CONCENTRATIONS IN BRAIN PARENCHYMA BEFORE AND AFTER SEIZURE ACTIVITY. A MICRODIALYSIS STUDY

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Objective: This study aims to record the alterations of cytokine concentrations in the extracellular fluid of various brain areas during continuous intracranial EEG recording, on patients with drug-resistant epilepsy.

Patients – methods: Twelve patients with drug-resistant epilepsy were operated for placement of intracranial electrodes, and subsequently they underwent continuous Video-EEG recording. Two or three microdialysis tubes were implanted along with intracerebral electrodes and samples were collected every 4 hours. The concentrations of 6 cytokines (IL-1 β , IL-6, IL-8, IL-10, IL-12 and TNF α) were measured in the extracellular fluid, using the flow cytometry method. Time diagrams were built, and descriptive statistics were performed to evaluate the influence on cytokine fluctuations of various factors such as implantation microtrauma, seizure activity and focus, gliosis and brain location.

Results: Cytokine values measured after 48 hours from implantation were considered as basic concentrations. The microtrauma effect was evident until 48 hours after implantation by raised concentrations of most cytokines, and even longer regarding IL-6. This was more profound in gliotic tissue, particularly by increases of IL-1 (p=0.004) and TNF α (p=0.029). Statistically significant differences were found in the basic levels of IL-1b in gliotic locations (p<0.001) and of IL-6 both in gliotic (p=0.012) and non-gliotic epileptic ones (p<0.001). The cytokine values were not affected by which specific cerebral lobe was investigated. A significant alteration of cytokine parenchymal concentration was found in the first day after epileptic activity considering IL-6 (p=0.046), while post-ictal fluctuation of IL-1 was significantly different in gliotic locations (p<0.001).

Conclusions: The cytokine values and inflammatory response to microtrauma are significantly different between "healthy" and "gliotic" areas. This is in accordance with the "traumatic" theory of epileptogenesis. The development of epileptic seizures altered the levels of IL-6 in both "healthy" and "gliotic" areas, and of IL-1 only in gliotic ones. These findings could imply that a vicious circle including neuroinflammation and epileptogenesis could be taking place, at least in gliotic areas.

EPILEPSY SURGERY FOR REFRACTORY EXTRATEMPORAL EPILEPSIES

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The surgical approach is an established method for treatment of refractory partial epilepsy. Especially, epilepsy that originates outside of the temporal lobe may present significant challenges in the patient with drug-resistant epilepsy.

The presurgical evaluation and the operative strategy in patients with extratemporal epilepsies are aiming to define the anatomic localization of the epileptogenic zone, the physiologic abnormality and the normal function of the area. These goals can be achieved using long term Video-EEG, high resolution structural and functional imaging techniques, neuropsychologic studies, invasive EEG monitoring when is necessary and cortical stimulation in the definition of eloquent cortical areas.

We present 41 patients, aged 14-43, 29 men and 12 women who were treated surgically for drug-resisting epilepsy of extratemporal origin. 11 patients suffered from non-lesional epilepsies. 30 patients suffered from lesional epilepsies which resulted from malformations of cortical development, vascular malformations, tumors and areas of old injury or surgery.

56% (23/41) of the patients are seizure free after the surgical procedure (follow-up 1-10 years). 7 patients show worthwhile seizures reduction and 9 patients do not show any appreciable improvement. One patient died 3 months after surgical procedure from lung cancer and one patient did not present at the follow-up.

EVALUATION OF DESYNCHRONIZING CONTINUOUS LOW- AND HIGH-FREQUENCY STIMULATION IN FULLY HIPPOCAMPAL KINDLED RATS

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Objective: Low and high frequency stimulation (LFS, HFS respectively) have been reported to inhibit the development of kindling and to modify seizure characteristics in rats. We here report the effects of hippocampal LFS and HFS applied at two or four sites in fully kindled rats.

Methods: Rats were implanted with a hippocampal tetrode and kindled until they reached to fully kindled state. Stimuli to evoke seizures were adjusted to individual afterdischarge (AD) thresholds. Stable animals were divided in 5 groups; stimulation at 1 Hz (LFS) or 130 Hz (HFS) was applied for seven days via 2 or 4 sites, effects were compared to a control group. Four-contact stimulation was performed in a rotatory fashion. The stimulation effect on the AD thresholds, duration and on behaviour was analysed.

Results: With stimulation via 4 sites, LFS consistently increased the AD threshold, and HFS significantly decreased the AD duration. No relevant alterations were observed in the 2-contact stimulation groups. No behavioural alteration was observed during the stimulation period.

Conclusions: These findings suggest that effects of hippocampal stimulation depend both, on topographical aspects of stimulus application and on stimulation frequency. Both LFS and HFS have an antiepileptic effect on afterdischarges when applied in a rotatory pattern. This supports concepts on patterned stimulation to result in desynchronization and in an antkindling effect. The results may be important for improved clinical applications of deep brain stimulation in the therapy of epilepsy.

QUALITY OF LIFE AFTER EPILEPSY SURGERY, A PROSPECTIVE STUDY

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Evaluation of quality of life in epilepsy is particularly important, while it is one of the common disabling chronic diseases. In this study, our aim is to evaluate postoperative changes in terms of seizure frequency, antiepileptic drug (AED) consumption and quality of life. Thirty patients who underwent epilepsy surgery (resective or palliative) because of medically intractable epilepsy are included in the study. Besides demographic feature, seizure frequency, number of AEDs is obtained, and SF-36 is administered pre- and post operatively. Anterior temporal lobectomy and amygdalohipocampectomy was carried out in 22/30, extra-temporal cortical resection in 2/30 and VNS in 6/30. Following mean follow up period of 19 months 66,6% of patients achieved Class I seizure control and a significant reduction in number of AEDs ($p < 0,005$). 5/8 subscales (general perception of health ($p < 0,05$), role limitations due to physical problems, role limitations due to emotional problems, emotional well being and energy ($p < 0,005$)) of SF-36 significantly improved postoperatively. Furthermore, there was an negative correlation between role limitations due to physical problems and postoperative AED number ($p < 0, 05$). In conclusion, surgical interventions for medically intractable epilepsy have low morbidity and significant benefit on quality of life. The common point of most studies in the literature is the reduction/cessation of the seizures is correlated with improvement in quality of life. Therefore, patients with medically refractory epilepsies should be directed to comprehensive epilepsy centers for presurgical workup more frequently.

Key Words: Epilepsy, surgery, quality of life

10/OP31

LONG-TERM HARDWARE-RELATED COMPLICATIONS OF HIPPOCAMPAL STIMULATION: EXPERIENCE FROM MEXICO CITY'S GENERAL HOSPITAL

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Objectives: To determine the long term hardware-related complications of hippocampal stimulation for the treatment of drug resistant epilepsy.

Methods: A retrospective analysis of all patients operated for hippocampal implantation of electrodes from June 1999 to July 2008 was performed. Fifteen electrodes were implanted in 11 patients, ages ranging 14-43 years, with no comorbidities.

Results: A total of 11 hardware-related complications occurred in 5 patients (45.45%) and 7 stimulation systems (46.66%) at a mean time of 48.29 (3 to 118) months after implantation. The mean follow-up period was 57.33 months with a minimum of 15 months. Complications included 2 electrode fractures (13.33%), 6 skin erosions (40%) being retromastoid the most common site, 2 infections (13.33%) and one wire tethering (6.66%). Complete removal due to infection was necessary for 2 stimulation systems (13.33%). One more system (6.66%) had to be removed due to recurring skin erosion and was reimplanted three months later.

Conclusions: Hippocampal stimulation has proved to be safe for seizure control in patients with drug resistant mesial temporal lobe epilepsy who are not suitable candidates for ablative procedures. At our institution hardware-related complications were more common than reported in the literature. Bone drilling along the retromastoid electrode trajectory might be a solution to skin erosion. It is important to identify other factors leading to complications in order to avoid them and improve patient outcome.

RADIOSURGERY

ORAL PRESENTATIONS

1/OR33

HYPOFRACTIONED STEREOTACTIC RADIOTHERAPY FOR VESTIBULAR SCHWANNOMAS. LOCAL CONTROL AND HEARING PRESERVATION.

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Objective. Aim of the present study is to evaluate the possible advantage of hypofractionated stereotactic radiotherapy both in terms of effectiveness and safety.

Patients and methods. All the 61 patients included in present study underwent a hypofractionated stereotactic treatment with a prescription dose of 18 Gy, in 3 fraction

All patients are classified according to the American Academy of Otorinolaryngology-Head and Neck Surgery classification.

In order to improve the target definition and to obtain more anatomic details about the critical structures the CT images were always fused with MRI.

Cranial nerve function, audiograms, and magnetic resonance images (MRI) were monitored 2 months after treatment and every 6 months thereafter.

The PTV was defined as the tumor volume without margin. The mean tumour volume was 4,5 cc (range 0,05-13,2cc; median 3,6cc). The mean dose to the cochlea was 16,3Gy to the 50% of the volume.

Results: the mean follow-up period was 35 months (range 23-60 months). Four patients died during the follow-up. One patient had a cerebral stroke and other three patients died due to unrelated causes.

The tumor growth control was achieved in 95% of the series. Eighteen percent had a partial response (shrinkage > 25%). Only the 5% of the patients showed a progression disease.

The 75 % of the patients maintained a serviceable hearing function.

Conclusions. This experience suggests that hypofractionated stereotactic radiotherapy by CyberKnife would be safe and effective. The tumor growth control was optimal and the hearing function preservation rate were promising.

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BRAIN CAVERNOMAS - LONG TERM RESULTS OF RADIOSURGERY

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Object. The radiosurgery of cavernomas remains a controversial indication. Long term results from our centre were evaluated.

Methods. 112 patients with brain cavernomas were treated using the gamma knife in Prague between 1993 and 2000. The marginal dose was a median of 16 Gy. Follow-up ranged 5-184, median 84 months. The risk of bleeding before radiosurgery was 2% annually. Overall a 1.4% risk of rebleeding was observed after gamma knife treatment, after latency interval of 3 years since the treatment risk of rebleeding was 0,5%. An increase in the volume of the cavernoma was observed in 7 (6%) of patients and a decrease in 58 (52%) after the treatment. Collateral oedema after radiosurgery was detected in 27% of patients, which, together with the rebleeding, caused temporary morbidity in 20.5% of patients and permanent morbidity in 4.5%. Risk of oedema increased with higher marginal dose and cavernoma volume. 39% of patients suffered from epilepsy before radiosurgery and this improved in 45% of them. In 4 patients radiosurgery on amygdalohippocampal complex was added for insufficient effect on epilepsy. Microsurgical resection of irradiated cavernoma was performed in 9 patients (8%) - 3 of them for persistent secondary epilepsy not effected with radiosurgery, 1 for postirradiation oedema and 5 for cavernoma rebleeding or volume progression. 3 patients with brain stem cavernoma died because of rebleeding or cavernoma progression.

Conclusions. In properly selected cases, radiosurgery can be considered as a treatment option for symptomatic brain cavernomas with high risk of microsurgery.

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LINAC-RADIOSURGERY WITH MINIMIZED DOSES FOR BRAINSTEM METASTASIS

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Purpose Treatment of cerebral metastases located inside the brainstem remains a challenge. We report a retrospective study of 30 consecutive patients treated in our institution between 2005 and 2007 with micromultileaf LINAC-radiosurgery for brainstem metastases, with reduced doses compared to those usually reported in the literature.

Patients and methods Mean follow-up was 311 days (41-958). Median age was 57 (37-82), Mean Karnofsky Index (KI) was 80. Primary tumor site was lung (n=13), breast (n=4), kidney (n=4), skin (melanoma) (n=3), others (n=6). Primary tumor was controlled in 17 cases; extra-cranial metastases were controlled in 12 cases. Median volume was 2.82 cc (0.06-18). Dose was delivered by a micromultileaf collimator BrainLab and a 6 MV- LINAC.

Results Dose administered at the 70% isodose was 13.4 Gy (8.2-15). Median survival was 10 months. Local control rates at 3, 6 and 12 months were 100%, 87% and 78% respectively. Neurological control rates at 3, 6 and 12 months were 69 %, 54.5 % and 20 % respectively. No parameter was found to significantly correlate with survival, local or cerebral control. No patients had severe side-effects (grade III-IV), according to RTOG scale.

Conclusion Lower doses than previously reported can achieve the same local control and survival rates in brain metastases, with minimal side-effects.

RADIOSURGERY OF MALIGNANT (ATYPICAL AND ANAPLASTIC) MENINGIOMAS

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Clinical entity of malignant (non-benign) meningiomas is well known and radiotherapy after total resection has been indicated in 1984 (Inoue et al. *Acta Neurochirurgica* 73: 179-191). Seventy three tumours in 45 patients with atypical and anaplastic meningiomas were treated with single or multisession radiosurgery. Clinical features and treatment results of atypical and anaplastic meningiomas were analyzed. Thirty two lesions in 25 patients with atypical meningiomas and 41 lesions in 20 patients with anaplastic meningiomas were treated and followed with median follow-up periods of 27.5 and 25 months, respectively. The median tumor volume and median marginal dose in both groups were 14.5ml vs. 7.2ml and 20Gy vs. 24Gy, respectively. The median prescribed isodose and median number of treatment session were 59% and 3 sessions in both groups. Five patients received retreatment for new recurrent tumours in each groups after median periods of 34 months and 8 months, respectively. Two patients with anaplastic meningiomas required resection surgery for recurrent tumours. Three-year survival rates of patients with atypical and anaplastic meningiomas were 91.7 and 85.9%, respectively. Four patients with anaplastic meningiomas died up to 43 months after treatment due to recurrences. Radiosurgery is effective for atypical and anaplastic meningiomas, especially for relatively small tumours. Close follow-up examinations with 3 to 6 months intervals are recommended for early detection of new recurrent lesions.

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VISUAL OUTCOME IN MENINGIOMAS AROUND THE ANTERIOR VISUAL PATHWAYS TREATED WITH FRACTIONATED STEREOTACTIC RADIOSURGERY .

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Background: Meningiomas threatening the anterior visual pathways (AVP) and non-amenable for surgery, are currently treated with multisession stereotactic radiation. Stereotactic radiation is available with a number of devices. The most ubiquitous include the Gamma knife, Cyberknife, Tomotherapy, and isocentric linear accelerator (LINAC) systems.

Objective: To describe a case series of AVP meningiomas treated with LINAC fractionated stereotactic radiosurgery (FSR) using the multiple, non-coplanar, dynamic conformal rotation paradigm, and to compare the success and complication rates with that reported for other techniques.

Methods: We included all patients with AVP meningiomas followed at our neuro-ophthalmology unit for a minimum of 12 months after FSR. We compared details of neuro-ophthalmological examinations and tumor size pre-and post radiation and at the end of follow-up.

Results: Of 87 patients with AVP meningiomas, 17 were referred for FSR. Sixteen patients completed more than 12 months' follow-up (mean 39 mo). Eleven had prior surgery, while 5 had FSR as first line management. Tumor control was achieved in 14/16 cases, with three meningiomas shrinking in size after radiation. Two meningiomas progressed, one of them in an area that was outside of the radiation field. Visual functions improved (6) or stabilized (8) in 14(88%) patients and worsened in two (12%).

Conclusions: Fractionated LINAC radiosurgery using the multiple non-coplanar dynamic rotation conformal paradigm may be offered to patients with meningiomas threatening the anterior visual pathways as an adjunct to surgery or as first-line treatment with results comparable to those reported with other stereotactic radiation techniques.

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VERY LONG-TERM RESULTS OF STEREOTACTIC RADIOSURGERY: SHOULD WE MODIFY OUR MANAGEMENT STRATEGY OF PITUITARY ADENOMAS?

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Objective: To determine long-term efficacy and adverse effects of GK in secreting pituitary adenomas. This is a retrospective study of patients treated by GK in the center of Marseille, France, with a follow-up at least equal to 60 months.

Patients: 76 patients were treated by GK for acromegaly (n=43), Cushing's disease (CD, n=18) or prolactinoma (n=15), as a primary (n=27) or adjunctive post-surgical treatment (n=49).

After withdrawal of antisecretory drugs, patients were considered in remission if they had mean GH levels < 2 ng/ml and normal IGF1 (acromegaly), normal 24h urinary free cortisol and cortisol < 50 nmol/l after low dose dexamethasone test (CD), or 2 consecutive normal samplings of prolactin levels (prolactinoma).

Results: After a mean follow-up of 96 months, 44.7% of the patients were in remission. Mean time to remission was 42.6 months. Twelve patients presented late remission at least 48 months after GK. Two patients with CD presented late recurrence 72 and 96 months after GK. Forty percent of patients treated primarily with GK were in remission. Target volume and initial hormone levels were significant predictive factors of remission in univariate analysis. Radiation-induced hypopituitarism was observed in 23% patients; in half of them, hypopituitarism was observed after a mean time of 48 to 96 months. Twenty-four patients were followed more than 120 months: rates of remission and hypopituitarism were similar to the whole cohort.

Long-term data confirm the anti-secretory efficacy of the procedure (about 50% remission in hypersecreting tumors) but also a previously unknown risk of recurrence (about 2-10% cases), in contrast with fractionated radiotherapy. The main drawback of the procedure is the time to remission estimated to range from 12-60 months. The anti-tumoral efficacy is observed in about 90% cases, taking into account both unchanged and decreased tumor volumes after the procedure. This latter point is of major importance for non-secreting slowly growing pituitary adenomas. Hypopituitarism is the main side-effect, observed in 20-40% cases.

Conclusions: GK is an effective and safe primary or adjunctive treatment in selected patients with secreting pituitary adenomas. All these data show that SR is probably still useful in the therapeutic algorithms of pituitary adenomas, despite the fact that antisecretory drugs, particularly for acromegaly, are becoming more and more effective and well tolerated.

7/OR39

INTEGRATION OF FUNCTIONAL MRI AND WHITE MATTER TRACTOGRAPHY IN STEREOTACTIC RADIOSURGERY

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Objective: To study the efficacy of the integration of functional MRI (fMRI) and diffusion-tensor-imaging (DTI) tractography data into stereotactic radiosurgery.

Methods: fMRI and tractography data were acquired, along with the high resolution anatomical MR images used in treatment planning for a number of selected patients treated with the CyberKnife system. All images were imported in the treatment planning system and used to delineate the treated lesions and the surrounding critical structures. Treatment plans with and without incorporating the delineated functional structures and the fiber tracts into treatment planning procedure were developed and compared.

Results: The nearby functional structures and fiber tracts could receive doses >50% of the maximum dose if excluded from the planning process. When considered, the dose received by these structures was reduced by up to 50%, depending on the relative distance from the treated lesions. In the case that the critical structures were bordering the treated target the required therapeutical dose was delivered by exploiting different fractionation schemes.

Conclusions: Functional structures and fiber tracts could receive high doses if not considered during treatment planning. With the aid of the fMRI and tractography images, they can be delineated and spared.

8/OR40

LEKSELL GAMMAKNIFE RADIOSURGERY FOR IDIOPATHIC TRIGEMINAL NEURALGIA: A NEUROVASCULAR ANATOMICAL STUDY.

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OBJECTIF

To study the anatomy of neurovascular compression in patients with idiopathic trigeminal neuralgia treated with Leksell gammaknife radiosurgery.

MATERIAL AND METHODS

On hundred and seventy five consecutive patients (81 men and 94 women) with proven medically refractory idiopathic typical trigeminal neuralgia, treated with Leksell gammaknife radiosurgery (Elekta Instruments, Stockholm, Sweden) in our institution between January 2004 and December 2008 were included.

Images acquisition was done with 1 mm thick CT-scan and 1 mm thick MRI, in both axial T1-weighted enhanced and axial T2-weighted with *Balanced Fast-Field Echo* (Achieva, Philips Medical Systems, Best, The Netherlands), with coronal and sagittal reconstructions.

Patients were treated using a single 4 mm shot to the retrogasserian cisternal portion of the trigeminal nerve, with a mean maximal GKS dose of 85 Gy (65-90 Gy).

Follow-up data were obtained by face-to-face interviews, using the Barrow Neurological Institute Pain Intensity Scale. The follow-up period ranged between 6 and 64 months (mean 21 months).

The anatomical analysis of the images was performed with the Gammaplan software (Elekta Instruments, Stockholm, Sweden). Neurovascular compression and morphometric data were recorded retrospectively by an independent observer, being blind of the treated side, and the territory of neuralgia.

RESULTS

In 80,5% of the patients a neurovascular compression was observed. A last follow-up, complete pain relief (BNI I to IIIa) was achieved in 61 % of the patient. Pain recurrence occurred in 11% of the patient. Grade III neurovascular compression or previous treatment was not associated with different outcome.

CONCLUSION

Visualisation of a neurovascular compression was not associated with pain outcome.

ORAL POSTERS

1/OP32

CYBERKNIFE RADIOSURGERY FOR THE TREATMENT OF SHORT-LASTING UNILATERAL NEURALGIFORM HEADACHE WITH CONJUNCTIVAL INJECTION AND TEARING (SUNCT). PRELIMINARY DATA

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Background/Aims: Short-lasting unilateral neuralgiform headache with conjunctival injection and tearing (SUNCT) is a subtype of trigeminal autonomic cephalalgia characterized by short-lasting attacks of sharp unilateral pain associated with conjunctival injection and tearing. The number cephalalgic attacks may reach 200/day and the pain can be elicited by stimulation of trigger points localized on the skin or the oral or nasal mucosae. Response to medical therapy is often poor and this exposes patients to severe, invalidating pain and dysautonomic symptoms.

The sphenopalatine ganglion (SPG) mediates the parasympathetic symptoms typical of trigeminal neuralgiform autonomic pain. The largest of the four parasympathetic ganglia of the head and neck, the SPG provides sensory and autonomic fibers to the lacrimal gland, paranasal sinuses, nasal cavity, pharynx, gums and palate. The preganglionic parasympathetic fibers from the greater petrosal branch of the facial nerve synapse inside the SPG with neurons whose postganglionic axons, vasodilator and secretory fibers, are distributed with the deep branches of the trigeminal nerve.

Radiosurgery may represent a relatively easy and low-risk alternative for the treatment of SUNCT. No radiosensitive structures are present nearby, and SPG tolerates up to 90 Gy without evident damage to neurological function. The supposed mechanism of response is related to the synaptic or axonal modulation of parasympathetic fibers axonal modulation/injury of afferent pain fibers.

Methods: Three patients with SUNCT underwent robotic radiosurgery. All patients had a long history of acute neuralgiform retro-orbital and maxillary pain with sudden onset and short duration followed by persistent aching and burning and dysautonomic features including conjunctival injection and tearing, miosis, ptosis, nasal discharge, vasomotor and trophic changes of the skin, hyperhidrosis. 3T MR revealed a thickening of the wall of the sphenopalatine fossa associated with a high signal intensity on T2 imaging. 3T imaging was essentially unremarkable in the other two patients. Treatment was delivered after radiosurgical planning based on CT-MR fusion. 3T MR allowed direct visualization of the SPG.

Results: The volume of the target averaged 0.3 mL. The first patient received a prescribed dose of 35 Gy to the 70% isodose line and became pain free, meds free after 2 months. No recurrent pain was observed in this patient during a 4 year follow-up. The second patient received a prescribed dose of 60 Gy to the 80% isodose line. This patient experienced a progressive improvement becoming pain free after 6 months and stopping the medications (he was assuming 1200 mg of carbamazepine daily before the treatment). A short period of recurrent pain was experienced after 1 year and controlled adding 200 mg of carbamazepine daily. The third patient is pain free 4 months after the treatment. No side effects were recorded to date.

Conclusions: SPG radiosurgery was found to be a safe and effective treatment for trigeminal neuralgiform autonomic pain. Doses higher than 60 Gy may be required for long term control. Overall safety and long term efficacy of SPG radiosurgery in selected patients should be investigated by a prospective trial

2/OP33

PRELIMINARY RESULTS OF LINAC - BASED RADIOSURGERY IN AVM AND CEREBRAL TUMOURS IN ONCOLOGICAL CENTER IN BYDGOSZCZ - POLAND

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Introduction: Efficacy of stereotactic radiosurgery in the treatment in cerebral AVM's, meningiomas, metastases, acoustic neuromas and recurrent anaplastic gliomas is well documented. The object of this work was the analysis of the results of the treatment of AVM and selected cerebral lesions with linear accelerator-based stereotactic radiosurgery.

Patients and methods: In a strict collaboration with Department of Neurosurgery of Military Clinical Hospital, in the Department of Radiotherapy of Oncological Center in Bydgoszcz, Poland since February 2009 until may 2010 45 patients with cerebral tumours and AVM's have been treated with linear accelerator-based stereotactic radiosurgery. There were 25 females and 20 males. The lesions included: 11 AVMs, 19 meningiomas, 11 metastases, 2 acoustic neuromas, 3 gliomas. A mean radiation dose of 16Gy was delivered to the tumour or AVM margin and 12 Gy to the tumours located in a ponto - cerebellar angle. Follow-up was 2 -15 months.

Results: Control of tumour growth was achieved in all cases after 6 months and radiological regression was observed in 12 cases after 12 months. There were no new permanent deficits nor complications after radiosurgery requiring medicamentation.

Conclusion: A longer follow-up is required to determine the long term efficacy and the toxicity of this treatment in our institution.

**CEREBRAL METASTASES OF BREAST CANCER TREATED BY
LINAC-Radiosurgery**

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Introduction. Cerebral Metastases arising from breast cancer are 5-20% of the patients and still represent a challenge. Given the fact that the course of this disease is slow when compared to other primary sites, it offers a particular opportunity to observe impact of radiosurgery on neurological control.

Results. We analysed retrospectively results of 113 patients treated between 2006 and 2009 by LINAC with BrainLab MMLC for 189 lesions. Mean age was 53, mean KI was 80. Mean interval between primary and cerebral metastases was 68 months. Mean number of lesions/patient was 1.6, mean total volume was 6.4 cc, mean RPA was II, mean SIR was 6. Mean dose at the 70% reference isodose was 16 Gy, mean maximum dose was 20.2 Gy. Crude local control was 89%. Median survival was 16.3 months. Multivariate analysis showed that age ($p<0.001$), number of metastases ($p=0.009$) and SIR ($p<0.001$) were significantly correlated with survival. Mean delay between radiosurgery and distal relapse was 10 months. The only predictor for distal control in multivariate analysis was number of metastases ($p= 0.007$).

Conclusion. In this study, number of metastases was correlated with survival and was the only predictor of distal relapse. The influence of neurological control on survival will be discussed.

MOVEMENT DISORDERS III

ORAL PRESENTATIONS

1/OR41

THE EFFECT OF DEEP BRAIN STIMULATION OF THE PALLIDUM AND THE SUBTHALAMIC NUCLEUS FOR CAMPTOCORMIA IN DYSTONIA AND PARKINSON'S DISEASE

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Objectives: Camptocormia may occur in various movement disorders such as primary dystonia or idiopathic Parkinson's disease (PD). There are only few data available on the effect of DBS on camptocormia comparing these two conditions.

Methods: Seven patients (4 with dystonia, 3 with PD; mean age 60.3 years at surgery, range 39-73 years) with camptocormia were included in the study. Five patients underwent bilateral GPi DBS and two patients underwent bilateral STN DBS. Pre- and postoperative motor assessment included the BFM in the dystonia patients and the UPDRS in the PD patients. Severity of camptocormia was assessed by the BFM subscore for the trunk at a mean last available follow up at 17.3 months (range 9-36 months).

Results: There were no surgical complications. In the four patients with dystonia there was a mean improvement of 53 % in the BFM motor score (range 41-79%) and of 63% (range 50-67%) in the BFM subscore for the trunk at the last available follow-up (mean 14 months, range 9-18 months). In the three patients with PD who underwent bilateral STN DBS (2) or pallidal DBS (1) the PD symptoms improved markedly (mean improvement UPDRS motor subscore stimulation on/medication off 55%, range 46-61%) but there was no or only mild improvement of camptocormia in the two patients who underwent STN DBS and only moderate improvement in the patient with GPi DBS at the last available follow-up (mean 22 months, range 12-36 months).

Conclusion: GPi DBS is an effective treatment for camptocormia in dystonia. The response of camptocormia to chronic STN or GPi DBS in PD is more heterogenous. The latter may be due to a variety of causes and needs further clarification.

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VENTRO-ORAL NUCLEUS THALAMOTOMY FOR TASK-SPECIFIC FOCAL HAND "OCCUPATIONAL" DYSTONIA

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[Background] Task-specific focal hand dystonia is often related with occupational use of the fingers among professional musicians, writers, barbers, and so on. Even if the symptom seems very minor to physicians, their professional life is jeopardized. The dystonic symptoms are generally refractory to most conservative treatment.

[Patients and Methods] Ninety-two patient with task-specific focal hand dystonia (writer's cramp: 67, musicians cramp: 20, barber's cramp: 4, Cook's cramp: 1) were treated with ventro-oral nucleus thalamotomy since 2001. Professional workers (23 patients) among the subjects were as follows; cartoon artist: 4, musician: 14, barber: 4, cook: 1.

[Results] During the mean follow-up period of 40 months (range:6-110), twenty professional workers (87%) had returned to previous professional activities. One musician, one barber, and the cook were not satisfied with the surgical results, and stopped their occupation. There were no permanent complications. The acquired skill for profession was not affected after surgery. None of the patients complained of difficulty of learning new activities like practicing new music. To control dystonic tremor, additional coagulation was required to the Vim nucleus.

[Discussion and Conclusion] Ventro-oral thalamotomy may be a last resort option, but it is safe and effective for task specific focal hand dystonia. Vo thalamotomy only affects dystonic symptoms, and does not have any effects on acquired skill and learning. There is no consensus whether such occupational dystonia can be controlled with deep brain stimulation (DBS). However, the authors' preference is ablative procedure for this particular condition, because most symptoms are unilateral, device related problems are not negligible in DBS, and ablation can bring "cure" to the patients. When the professional life is threatened with focal hand dystonia, Vo thalamotomy can be suggested to the patients.

PALLIDAL HIGH FREQUENCY STIMULATION IN MEIGE SYNDROME – LONGTERM CLINICAL EFFECTS IN A MULTICENTER RETROSPECTIVE ANALYSIS

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Objectives: While pallidal high frequency stimulation (GPI-HFS) is effective in the treatment of segmental and generalized dystonias, its longterm effects on Meige syndrome, a particular craniofacial segmental dystonia is unknown. We retrospectively assessed the clinical efficacy of GPI DBS in 12 patients with Meige syndrome from three German movement disorders centers for up to 78 months.

Methods: Dystonia severity, based on the video documentation of the pre- and postoperative neurological examinations was assessed on the Burke Fahn Marsden Dystonia Rating Scale (BFMDRS), the Blepharospasm Movement Scale (BMS) and the Abnormal Involuntary Movement Scale (AIMS).

Results: We followed 6 men and 6 women with a mean age of 64.5 ± 4.4 years at surgery and a mean disease duration of 8.6 ± 4.4 years. The BFMDRS showed a mean improvement of 45% at short term follow-up (4.4 ± 1.5 months; $p < 0.001$), and of 53% at long term follow-up (38.8 ± 21.7 months; $p < 0.001$). BFMDRS subscores were improved for eyes by 38% ($p = 0.004$) and 47% ($p < 0.001$), for mouth by 50% ($p < 0.001$) and 56% ($p < 0.001$) and for speech/swallowing by 44% ($p = 0.058$) and 64% ($p = 0.004$). The mean improvement in the BMS was 25% ($p = 0.006$) and 38% ($p < 0.001$), and in the AIMS 44% ($p < 0.001$) and 49% ($p < 0.001$).

Conclusions: Our retrospective multicenter case series demonstrates GPI DBS to be a longterm safe and highly effective therapy for Meige syndrome.

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PYRAMIDAL SYSTEM STIMULATION FOR THE TREATMENT OF FIXED DYSTONIA

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The fixed dystonia syndrome is a pathological condition whose aetiopathogenesis and its organic correlations are still obscure; several groups have hypothesized the existence of "fixed psychogenic dystonia" as a subgroup of the syndrome, distinguishable from the organic form by the presence of more or less clear-cut psychological symptoms that can be related to the dystonia.

Other groups have focused their attention on the neurophysiological correlates of the whole "fixed dystonia" group and on the difference between the them in the so-called psychogenic and organic groups.

We report our experience with 12 patient submitted to stimulation of the internal capsule's posterior limb (three patients) and of the motor cortex (9 patients) for treatment of fixed post-stroke appendicular dystonia . Long-term results have been encouraging, showing the role of the stimulation of the pyramidal system for this condition.

5/OR45

**A PROBABILITY ATLAS OF THE THALAMUS FOR STEREOTACTIC NEUROSURGERY:
A STUDY OF THALAMIC ANATOMY AND GEOMETRY**

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Introduction

Stereotactic targeting of thalamic structures is performed for Deep Brain Stimulation (DBS) or lesional surgery for a variety of conditions including movement disorders and chronic pain. Individual thalamic nuclei are difficult to visualize on standard MR sequences. Generic stereotactic coordinates are used for various nuclei in stereotactic neurosurgery. We analysed the anatomical variability in position, shape and volumetry of the thalamus using 300 MR brain images, to determine the suitability of generic stereotactic target coordinates

Methods

MR imaging data of 300 healthy subjects was analysed. After affine registration, segmentation of the thalamus was performed using a probabilistic adaptation of the active appearance model. Segmented images were then used to create a probability atlas of the thalamus. A multivariate Gaussian model of vertex location and intensity variation was then applied, using point correspondence across subjects. Correlation of thalamic vertices with age was performed using F statistics.

Results

3-dimensional thalamic cartesian coordinates were calculated. Significant variability of thalamic anatomic location was evident, with stereotactic concordance above 95% demonstrated in a limited distribution. The centre-of-mass (centroid) was measured and laterality of centroids was demonstrated to correlate with subject age ($p < 0.001$), and thalamic volumetry ($p < 0.001$). Laterality increased with reduced cortical grey matter volume and total brain volume ($p < 0.001$). Geomatic analysis of thalamic vertices demonstrated inward movement of vertices with age, confirming regional atrophy, and affecting centroid laterality. Medial movement of vertices was demonstrated at the anterior pole and when adjusting for atrophy, a geometric shape change of the thalamus was noted with age.

Conclusions

This study demonstrates significant variability of thalamic anatomy in a large cohort of normal subjects. Centroid laterality correlated with subject age, brain atrophy and thalamic volume. Centroid laterality was due to regional atrophy and geometric change with an inward movement of the anterior pole and lateral movement of the body of the thalamus. Anatomical variability of this structure should be noted by neurosurgeons during the planning of stereotaxy as reliance on generic stereotactic coordinates for all patients is suboptimal.

ORAL POSTERS

1/OP35

MICROGRAPHIA INDUCED BY BILATERAL PALLIDAL DEEP BRAIN STIMULATION FOR SEGMENTAL DYSTONIA

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Objectives: Pallidal deep brain stimulation (DBS) has been established as an effective and safe method for refractory DBS. Parkinsonism due to lesions in the globus pallidus internus (GPi) has been reported in single cases secondary to brain hypoxia, after pallidotomy and recently also following DBS of the GPi. We evaluated and measured the degree of micrographia induced by bilateral chronic DBS of the GPi in patients with segmental dystonia using pre- and postoperative samples of handwriting.

Methods: We analyzed the height and width of a prespecified handwriting sample in 11 patients (mean age 57.6±13.6 years) preoperatively and at a median of 7 months (FU1; range 4-10) and 17 months (FU2; range 12-22) post DBS surgery. All patients had significant improvement in dystonic symptoms. None of the patients had involvement of distal arm and hand function in dystonic symptoms, and none reported typical capsular effects with GPi-DBS.

Results: Height of handwriting characters significantly decreased from 15.7±4.0mm (mean±SD) preoperatively to 13.5±4.1mm at FU1 (p=0.036) and 12.5±2.2mm at FU2 (p=0.008), and width of the handwritten phrase sample decreased from 121.3±36.1mm preoperatively to 105.8±33.5mm at FU1 (p=0.013) and 103.6±33.7mm at FU2 (p=0.009). The decrease in height and width did not correlate with stimulation intensity at FU1 and FU2 (height: r=0.13; p=0.57; width: r=-0.06; p=0.78).

Conclusions: Chronic bilateral GPi-DBS significantly decreases height and width of a standardized handwriting sample in patients with segmental dystonia. We postulate that this phenomenon reflects a disturbance of basal ganglia function in terms of hypokinetic syndrom as a side-effect of chronic bilateral GPi-DBS.

PALLIDAL STIMULATION FOR THE TREATMENT OF MEDICALLY-REFRACTORY DYSTONIA: OUR EXPERIENCE

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Objective: Deep Brain Stimulation (DBS) is an established treatment for various movement disorders, including dystonia. Different phenotypes and types of the disease demonstrate variable response to pallidal DBS. Our aim is to present the results of our department in treating dystonic patients with predominantly axial symptoms by DBS using quadro-polar constant-voltage electrodes.

Methods: We reviewed the medical history, treatment and outcome_data from all patients that received GPI-DBS for dystonia in our department. Outcome was evaluated using standard assessments, such as the Burke-Fahn-Marsden dystonia rating scale.

Results: The presented series includes 7 patients with dystonia who were treated with bilateral GPI-DBS. Mean age was 34.4 (range 21-48). The series included 5 cases of idiopathic dystonia (1 patient with camptocephalia, 2 patients with camptocormia, 1 patient with generalized dystonia and 1 patient with dystonic torticollis) and 2 cases of secondary dystonia, one ectatocormia owing to perinatal hypoxia and one camptocephalia secondary to Wilson's disease. With respect to idiopathic dystonias, the patient with camptocephalia improved by 86% in the TWSTRS. Camptocormia responded strikingly well, with a 100% improvement in the BFMDRS in both patients. The patients with generalized dystonia and torticollis improved by 55% and 10% respectively. In regard to secondary dystonias, the ectatocormia patient showed a remarkable improvement of 86%, whereas the patient with camptocephalia due to Wilson's disease improved by only 10%.

Conclusions: Deep Brain Stimulation by a quadripolar constant-voltage electrode is an effective treatment for dystonia. Patient selection has to be done on a case-by-case basis, as specific forms or certain phenotypes of the disease seem to respond better than others. Nonetheless, the final therapeutic result is multifactorial. Further studies are needed in order to determine better selection criteria of patients to be subjected to DBS treatment.

STIMULATION INTENSITY OF CHRONIC DEEP BRAIN STIMULATION CAN BE SIGNIFICANTLY REDUCED AFTER PULSE GENERATOR REPLACEMENT DUE TO END OF BATTERY LIFE IN PATIENTS WITH SEGMENTAL DYSTONIA

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Objectives: To maintain efficacy of DBS on segmental dystonia symptoms, incremental increase of stimulation intensity may be necessary over time. So far, no data are available regarding the adjustment of stimulation parameters after IPG replacement to achieve sustained optimal control of dystonic syndroms with least side effects.

Methods: We analyzed stimulation before and after IPG replacement in 17 consecutive and regularly followed-up patients with segmental dystonia. 14 patients had chronic DBS of the GPi, two patients of the Vim, and in one patient DBS was switched from GPi to Vim during follow-up.

Results: In 17 patients 40 IPGs were replaced: in 12 patients both IPGs were replaced in a single operation, in 6 of these twice until now, and in 2 patients IPGs were replaced consecutively. Mean IPG lifetime was 25±8 (range 18-50) months.

Optimal control of segmental dystonia was achieved at a mean stimulation intensity of 4.9±1.2V immediately prior to IPG replacement, which could be significantly reduced to 3.7±0.7V after replacement. Mean stimulation intensity prior to IPG replacement was higher with bipolar than with monopolar stimulation (5.2±1.1V vs. 3.9±0.6V), but reduction of stimulation intensity after IPG replacement was not significantly different in both stimulation modes (19.3% vs. 24.3%). In the six patients with a second replacement of IPGs, stimulation intensity prior to both replacements was comparable (5.1±1.0V vs. 5.0±0.8V).

Conclusions: Stimulation intensity can be significantly reduced after IPG replacement in patients with segmental dystonia irrespective of monopolar or bipolar stimulation mode. Subsequently, again an incremental increase of stimulation intensity is necessary. These mechanisms point at ongoing neuroplastic phenomena.

STATUS DYSTONICUS SECONDARY TO PANTOTHENATE KINASE-ASSOCIATED NEURODEGENERATION TREATED WITH PALLIDAL DEEP STIMULATION

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Introduction

Pantothenate kinase-associated neurodegeneration (PKAN), previously called Hallervorden-Spatz disease (HSD), is a rare disorder characterized by progressive motor dysfunction and dementia. Dystonia is the most prominent and disabling symptom, responding only to a modest extent to pharmacological therapy; some patients may present status dystonicus (SD), that is characterized by generalized muscle contractions resulting in life-threatening swallowing and respiratory disability.

Patient

A 18-years-old boy with a severe generalized dystonia had been diagnosed previously of Pantothenate kinase-associated neurodegeneration (PKAN). Brain magnetic resonance imaging (MRI) revealed the 'eye of the tiger' sign, and *PAVK2* mutation was detected by sequence analysis. The patient required several admissions at ICU due to status dystonicus. During last admission at ICU deep brain stimulation with general anaesthesia was realized. Microrregistration was eased by controlling anaesthesia with bispectral index. Electrodes were positioned in GPi bilaterally; a MRI revealed correct position of electrodes. A terrific improvement was observed, with cessation of dystonic storm and quick amelioration of the symptoms; Burke classification at discharge was 31/7, and after six months 20/6.

Discussion

Previous reports have proved the improvement of dystonic symptoms in patients with PKAN, specially in pediatric population, although improvement may delay. Status dystonicus may be a lethal complication of several neurological disorders with dystonia. Clinical response of status dystonicus due to PKAN with bilateral pallidotomy had been reported. As far as we know this is the first patient with status dystonicus due to PKAN treated successfully with deep brain stimulation.

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SPECIAL CONSIDERATIONS ON INTRATHECAL BACLOFEN FOR THE TREATMENT OF SECONDARY DYSTONIA

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OBJECTIVE

Intrathecal baclofen (ITB) infusion has emerged as a viable option for the treatment of the dystonic form of cerebral palsy. However, the application of ITB treatment in dystonia appears to be more challenging compared to the ITB for pure spasticity in cerebral palsy.

METHOD

We reviewed the records of 14 patients treated with ITB treatment for secondary dystonia. There were 13 males and 1 female with a mean age of 31 years. A literature review was also performed.

RESULTS

Higher baclofen doses (100µg) were necessary for a positive trial test in 8 patients (57%) and in 2 cases (14%) continuous infusion was necessary rather than single shot tests. Following implantation of the pump, 10 patients (71%) had significant improvement of the dystonic symptoms, while the remaining 4 patients (28%) showed small improvements and are candidates for adjuvant treatments. An unexpectedly high complications rate was observed compared to patients who received an ITB pump for spasticity; four patients (28%) needed pump revision, but following this, their clinical course was satisfactory.

CONCLUSION

Strategies to reduce complications and to make ITB treatment for dystonia more effective will be discussed. The presence of a dystonic element in patients with cerebral palsy makes the ITB treatment more demanding. Adjuvant treatments, such as oral medications and possibly DBS, might offer further improvement.

6/OP40

RAPID BODY WEIGHT LOSS IN PARKINSONIAN AND DISTONIC PATIENT-REVERSED AFTER FUNCTIONAL SURGERY.

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Introduction

Weight loss is common in Parkinson's disease (PD) and dystonic patients. This could influence morbidity and even mortality. Surgical approach is beneficial .

Method

Subjects

A 61 years lady with PD was admitted with "on medication" induced severe dyskinesias. Despite all conservative therapy, she lost 22 kg during the last 6 month. Her body weight index was 18.1 when admitted before surgery. She was operated – a bilateral subthalamic deep brain stimulator (DBS) was implanted with good results.

Another lady, 39 years old, presenting a painful advanced right side hemidystonia, lost 24 kg in the last 4 month despite a significantly supplementary oral diet. She was unable to sleep or even rest due to her movements. Her body weight index was 18.1 when admitted before surgery. A unilateral pallidotomy improved her.

Weight was measures before surgery and monthly after surgery for at least 6 month in both patients. To determine whether increasingly severe movement disorder is related to to greater weight loss we used a correlation analysis.

Results

Motor severe impairment improved in both patients. A progressive gain of weight was recorded.

Discussion

Mechanisms of weight control in severe movement disorders are unclear. They are probably multifactorial and elevated energy expenditure is included (correlation 0,82).

Conclusion:

When food intake and conservative therapy are overwhelmed by consumptive mechanisms, functional surgery is the only remaining solution to the problem.

MOVEMENT DISORDERS IV

ORAL PRESENTATIONS

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SUBTHALAMIC NUCLEUS DEEP BRAIN STIMULATION FOR YOUNG ONSET PARKINSON'S DISEASE

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Objective: Young Onset Parkinson's Disease (YOPD) refers to PD diagnosed between the ages of 21 and 40 years and faced different clinical phenomenology and management strategies. We assess the effectiveness of subthalamic nucleus deep brain stimulation in two groups of patients.

Methods: Among consecutive 90 PD patients with bilateral STN-DBS in our hospital from February 2003 to April 2010, twenty one YOPD patients and sixty nine idiopathic PD (iPD) comparatives were enrolled (mean age during operation: 32.8 ± 6.9 versus 53.2 ± 6.9 years old). The mean post-operative follow up was 26 ± 19.3 (3~60) months.

Results: The post-operative UPDRS total scores, part I, part II, part III and part IV in DBS on/med off all showed significant improvement ($p < 0.05$) comparing to pre-operative med off baseline in both groups without inter-group differences. However, axial scores in post-operative off stimulation and off medication seem to be getting worse in YOPD group. The neuropsychological evaluation both did not reveal deterioration in mini-mental status exam and Beck Depression Inventory. The stimulation parameters also are similar in two groups. In terms of complication, there were more YOPD patients with stimulation-related dyskinesia and hypomania but iPD with hypophonia. Three YOPD had stimulation related neuropsychological sequelae including hedonistic homeostatic dysregulation, mania, and impulse control disorder, which requiring psychiatric consultation.

Conclusions: Bilateral STN-DBS has comparable long-term benefit for YOPD. However, higher stimulation-related dyskinesia and neuropsychiatric issues and longer disease progression per se deserves more attention in this specified group.

2/OR47

LONG-TERM FOLLOW-UP OF UNILATERAL SUBTHALAMIC STIMULATION IN THE TREATMENT OF TREMOR DOMINANT PARKINSON'S DISEASE.

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Objectives:

The aim of this study is to evaluate the efficacy and safety of unilateral subthalamic stimulation in the treatment of advanced tremor dominant Parkinson's disease in the long-term follow-up.

Methods:

The study population is composed of 13 patients with idiopathic Parkinson's disease after unilateral subthalamic stimulation. The patients were operated on in local anesthesia with intraoperative electrophysiological target confirmation. The stereotactic target - the sensorimotor part of the subthalamic nucleus was calculated according to the midcommissural point derived from fusion of stereotactic computer tomography images with magnetic resonance images. The DBS leads (Type 3389 or 3387) were implanted with fluoroscopic guidance. The formal objective assessment included Unified Parkinson's Disease Rating Scale (UPDRS), Hoehn & Yahr Scale, and Mini Mental State Examination.

Results:

The follow-up period reaches in some patients 7 or even 8 years. The shortest follow-up period is 6 months. The patients are scheduled for postoperative follow-up visits at 3, 6, and 12 months and annually thereafter. On average 3 to 5 years after unilateral subthalamic stimulation 11 patients underwent contralateral ablative procedures including 8 thalamotomies and 3 pallidotomies. During presentation the results of patients with unilateral subthalamic stimulation and additional ablative procedures will be presented according to the above mentioned objective scales.

Conclusions:

Unilateral subthalamic stimulation is an effective and safe treatment for patients with tremor dominant Parkinson's disease. Most patients require second side surgery because of PD sings progression.

3/OR48

SACCADOMETRY: A NOVEL TOOL TO QUANTIFY THE MOTOR EFFECTS OF SUBTHALAMIC NUCLEUS STIMULATION IN PARKINSON'S DISEASE

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Introduction: High frequency stimulation of the subthalamic nucleus (STN HFS) is the therapy of choice in the surgical management of patients suffering from advanced Parkinson's disease (PD). At present, there is a compelling need for a rapid method of assessing its therapeutic effect that is ideally also target-specific, objective, automated, quantitative, and with high overall reliability. In this study we investigated the application of saccadic eye movements as a tool for assessing the therapeutic motor effects of STN HFS in patients with advanced PD.

Methods: Patients received bilateral STN HFS and were evaluated using saccadometry in all combinations of stimulation and medication on and off conditions, together with conventional motor assessments under the same conditions.

Results: We found that saccadometry can provide a sensitive and objective measure of the effects of STN HFS in PD patients that correlates well with conventional, subjective, evaluation of motor impairment.

Conclusions: Our findings identify the potential of saccadometry as a clinical tool for rapid and objective evaluation of the motor effects of STN HFS in PD patients.

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IS DEEP BRAIN STIMULATION A REVERSIBLE THERAPY? AN OFF-STIMULATION STUDY IN DYT1 GENERALIZED DYSTONIA

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Objective:

To study the clinical evolution during deep brain stimulation (DBS) discontinuation in a homogeneous group of DYT1 dystonia patients who are chronically benefiting from bilateral internal globus pallidus (GPi) stimulation and the factors influencing the clinical evolution in OFF-DBS.

Methods:

Eleven patients (8 female, mean age 27.5 years) with generalized dystonia followed for DBS therapy for at least 4.5 years were enrolled in the study. Clinical assessment was administered by two individual evaluators at three time points, separated by an interval of 48 hours. DBS conditions were as follows: ON, OFF1 (after immediate DBS switch-OFF) and OFF2 (after 48 hours DBS switch-OFF). The average scores between the two evaluators have been used for further analysis.

Results:

Significant difference has been found between ON-DBS condition and OFF1 ($p=0,032$). No significant difference has been found nor between ON-DBS and OFF2 ($p=0,067$) neither between OFF1 and OFF2 ($p=0,082$). None of the patients returned to the preoperative severity of dystonia scores. In three patients, dystonia did not worsen after 48 hours of DBS cessation.

The higher the current level in the ON condition for DBS, the more severe was the global worsening of dystonic symptoms (global movement scores) in OFF1 and OFF2.

Conclusion:

GPi DBS could be discontinued in DYT1 patients who were chronically treated with DBS for 5 years. Changes induced by the long term DBS could explain the lack of worsening in several patients when DBS was discontinued for 48 hours. The current drain seems an important parameter for clinical evolution when DBS is discontinued.

SUBTHALAMIC NUCLEUS DEEP BRAIN STIMULATION FOR GENERAL DYSTONIA TREATMENT.

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Medical treatment of generalized dystonia (GD) is frequently ineffective and surgical treatment of GD, where globus pallidus is a target is well accepted. The role of subthalamic nucleus as a target for deep brain stimulation for alleviating dystonic symptoms is not established yet. The authors present a group of patients treated with bilateral subthalamic deep brain stimulation (STN DBS).

Materials and methods: One patient who underwent previously bilateral pallidotomies and seven patients with identified PANK-2 mutation were qualified to STN DBS and surgically treated with deep brain stimulation between 2008 and 2010. Age of the patients varied from 8 to 32 years. The clinical condition of the patients was evaluated with various scales. At all cases the permanent electrodes were implanted to the subthalamic nuclei. The surgical procedure was undertaken under general anesthesia. The target was identified with direct and indirect method. Intrasurgical macrostimulation and microrecording were used for neurophysiological evaluation of the target. Postsurgical local field potentials were recorded in all cases.

Results: Neither neurological deterioration nor surgical complication were reported among the group. Caregivers of the patients noted subjective improvement of the clinical state of the subjects that was confirmed with tailored scales.

Conclusions: Subthalamic deep brain stimulation reduces abnormal dystonic movements. The technique carries minimal surgical risk, and improves quality of life of the patients.

Key words: NBIA, PKAN, PANK2, deep brain stimulation, subthalamic nucleus.

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VIM TARGETTING AND DTI IN GAMMA KNIFE SURGERY FOR INTRACTABLE TREMOR : INFLUENCE OF THE SHOT TOPOLOGY ON THE SAFETY EFFICACY.

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Introduction

Although DBS remains the gold standard in surgical treatment for movement disorders, the Vim GKS is becoming an attractive method for tremor with predominant upper limb involvement. This study evaluated the relationship between targeting method and patient outcome.

Materials and Methods

Between April, 2004 and October, 2009, 36 consecutive cases (26 males, 10 females, mean age 71) of invalidating tremor were treated in Timone University Hospital. Patients underwent imaging, including CISS MR ventriculography for targeting and DTI for capsula interna sparing. Vim was targeted (single 4-mm isocenter with a maximum dose of 130Gy) using Guiot method and adjusted using DTI to calculate the final dosimetry. Patients were followed with serial MRIs and clinical evaluations (Whiget tremor scale and functional scale) at 3 months, 6 months, 1 year and 2 years.

Results

Among 36 patients, 25 patients had essential tremor (1 patient post DBS) and 11 patients had Parkinsonian tremors. Follow-up was greater than 6 months for 20 patients (range 6-36). Target was left in 26 cases (72%) and right in 8 cases (28%). Outcome was excellent in 11 patients (55%) had outcome (>75% improvement in symptoms), 6 patients (30.0%) had good outcome (50-75% improvement), and 3 patients (15%) had failed outcome (less than 50% improvement). The symptom started to improve at 1 to 3 months, and at 6 months, 70% (14/20) of patients showed improvement. Follow-up MRI showed T2-hyperintense signal changes and mild gadolinium enhancement at 3 months and variable marked residual cavity after 1 year. One patient developed transient hemiparesis, who showed extensive hyperintense signal changes on the follow-up MRI. We analysed the distribution of our target coordinates in coronal, axial and sagittal planes from mid AC-PC line. We failed to demonstrate any significant correlation between the topology of the shot and the risk of failure or side effect may be due to the small size of the population.

Conclusion

Risk of failure or toxicity may be more depending on the pathophysiology of the tremor and/or genetic individual factors. However, an other explanation may be other factors related to patient selection or genetic predisposition. GKS with Vim targeting could be efficient and safe procedure in intractable tremor of predominant unilateral tremor patients.

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HIGH FREQUENCY STIMULATION OF THE STN IN PARKINSON'S DISEASE INCREASES GLOBAL CEREBRAL BLOOD FLOW

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Introduction

Subthalamic nucleus (STN) deep brain stimulation (DBS) is an effective therapy for Parkinson's disease (PD) but its therapeutic mechanism is not understood. Herein, we report a novel physiological effect of STN DBS: a global increase in cerebral blood flow (CBF).

Methods

Seven right-handed PD subjects with bilateral STN-DBS implants underwent CBF studies using H₂¹⁵O PET. Complete studies (12 whole-brain scans) were obtained on different days with the devices *on* and *off*. CBF was measured with large regions of interest that included all of the brain area in each transverse slice. CBF was determined using averages based on three criteria to estimate whether effects were driven by the highest flow rates, flow rates approximating gray matter, or flow rates combining gray and white matter: maximum voxels, upper 10% voxel values, 100% voxel values.

Results

CBF was higher when STN-DBS was *on* [$F(1,6) = 17.31, p = 0.006$] for each measure in all subjects. All subjects showed decreasing CBF over time in the *off* condition but not in the *on* condition [$F(2,12) = 13.86, p < 0.002$]. The magnitude of the CBF effect increased with the subject's levodopa dose and was related to the subject's speech timing.

Conclusions

STN-DBS appears to produce a significant increase in CBF that persists for hours after stopping stimulation. It is consistent with previous animal studies of subthalamic stimulation and with human studies on the vasoactive properties of levodopa. The effects of STN-DBS on cerebrovascular control warrant further attention.

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BILATERAL STIMULATION OF THE CAUDAL ZONA INCERTA NUCLEUS IN THE MANAGEMENT OF ESSENTIAL TREMOR

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Background

The Vim nucleus of the thalamus is the commonly chosen target for Deep Brain Stimulation in the treatment of medically refractory essential tremor (ET). Bilateral stimulation of this nucleus however, is associated with a high incidence of dysarthria and disequilibrium. We present our outcomes using bilateral stimulation of an alternative target, the caudal zona incerta (Zi).

Methods

We implanted bilateral MRI-guided Zi electrodes in 15 patients with ET. The Fahn-Tolosa-Marin Tremor Rating scale was used to assess tremor and the SF-36 healthy survey used to assess quality of life following surgery up to a follow-up period of 84 months. Operative and stimulation-related complications were recorded.

Results

The total tremor score improved by 73.8% (baseline mean score of 63.9 ± 16.2 to 16.7 ± 9.3 , $p < 0.0001$). The Part A score (Item 1-9) improved by 86.6% (baseline mean score of 21.5 ± 9.8 to 2.9 ± 2.9 , $p < 0.0001$).

The combined posture and action component tremor scores improved by 86.1% (from a mean baseline score of 9.6 ± 4.4 to a score of 1.4 ± 1.7 , $p < 0.0001$).

The Part B score (Item 10-14) which evaluates the functional activities of the upper limbs improved by 60.1% (baseline mean score of 24.7 ± 5.9 to 9.9 ± 3.9 , $p < 0.0001$). Part C score (Item 15-21), which evaluates the activities of daily living improved by 80.0% (mean baseline score 2.5 ± 1.2 to 0.5 ± 0.8 , $p < 0.0001$).

The SF-36 physical component score improved by 23.7% and the mental component score by 22.4%. There was one wound infection and 3 patients developed stimulation related dysarthria. None of the patients developed any disequilibrium or tolerance to stimulation.

Conclusion

Bilateral caudal Zi stimulation is safe and effective in suppressing medically refractory ET with good long term outcome.

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LONG-TERM SYMPTOMATIC IMPROVEMENT IN A CHILD WITH LESCH NYHAN SYNDROME TREATED WITH PALLIDAL DBS: REPORT OF A CASE AND REVIEW OF WORLD EXPERIENCE

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Lesch Nyhan syndrome (LNS) is an inborn metabolic disease characterized by severe generalized dystonia and self-mutilation behavior. We presented our 2-year experience with a child with LNS who maintains impressive symptomatic improvement with bilateral pallidal deep brain stimulation (DBS).

Clinical Material:

Our patient was diagnosed with LNS at 18 months. His generalized dystonia was noted at infancy; the self-mutilating behavior started at age 4 with finger biting and lower lip traumatic amputation. An intrathecal baclofen (ITB) provided symptomatic improvement of severe dystonia with episodic hyperthermia and rhabdomyolysis, but the pump was removed due to infection soon after implantation.

Based on encouraging published results in 4 patients from Japan, Switzerland and France, we implanted bilateral pallidal DBS device under general anesthesia in one sitting at the age of 7 years and 10 months.

Results:

Within 3 months after DBS initiation, dystonia improved and self-mutilation behavior markedly decreased so that restraints were no longer required. Although improvement in dystonia was similar to that with ITB, behavioral changes were unique to DBS treatment. A positive dynamics of symptomatic improvement continues during ongoing follow-up for 24 months after surgery.

We surveyed worldwide centers that reported DBS for LNS patients and found that all three patients from centers that responded to our survey continue using DBS maintaining symptomatic improvement many years after the implantation.

Conclusion:

Pallidal DBS appears effective in treatment of motor and behavioral symptoms of LNS. Our experience and that from other centers worldwide suggests that DBS offers long-term relief in LNS patients.

ORAL POSTERS

1/OP41

CHOREA INDUCED BY ELECTRICAL STIMULATION OF THE SUSTANCIA NIGRA IN PARKINSON'S DISEASE PATIENTS

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We present two cases of chorea due to misplacement of subthalamic stimulation electrodes.

Case 1: 47 male patient with Parkinson's disease starting with left bradykinesia. Three years later he presented very intense bradykinesia episodes with excruciating pain, partially alleviated by continuous infusion of apomorphine. As the patient met all criteria, DBS electrodes were implanted in both subthalamic nuclei. The electrical stimulation of the right DBS electrode, with very low voltages and a latency of 5 minutes, resulted in intense choreic movements of the four limbs. The movements were of great amplitude and increasing frequency. When the stimulator was off, the choreic movements ceased in 10-15 minutes.

Case 2: 62 old woman with Parkinson's disease of eighteen years course. The patient underwent DBS surgery with electrode implantation in the subthalamic nuclei. When the stimulator was on a similar picture to case 1 was observed.

RMI showed misplacement of the DBS electrodes. The neuronavigation system evidenced the bottom contact of the DBS electrode placed within the substantia nigra. In both cases we found that the anchorage system to the skull was flawed allowing the displacement of the electrode down the brain. Once the misplacement was corrected the two patients showed a good motor response.

The electrical stimulation of the substantia nigra, though uncommonly, may induce very intense choreic movements.

2/OP42

EIGHT YEARS FOLLOW-UP OF BILATERAL SUBTHALAMIC NUCLEUS STIMULATION IN ADVANCED PARKINSON'S DISEASE

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The short and medium term benefits of SubThalamic Nucleus stimulation (STNs) in patients with advanced Parkinson's disease (PD) are well documented. Long-term benefits have to be thoroughly investigated.

Objectives: This study provides a 8-year follow-up of PD patients under chronic STNs.

Methods: Nineteen consecutive PD patients were prospectively assessed yearly for eight years after bilateral STN implant. Parkinsonian motor symptoms were evaluated with (on) and without (off) levodopa treatment, with and without bilateral stimulation. Disease-related disability, neuropsychological and mood changes were comprehensively studied.

Results: Aborted procedures and intracranial haemorrhage complicated 2 implants, seizures recurred in 1 case, hardware complications in another one patient, six subjects died. In the remaining : (i) parkinsonian motor symptoms (Unified Parkinson Disease Rating Scale (UPDRS) III) were improved by STNs in "off" drug (by 48%) but none in "on" drug with respect to baseline pre-surgical "off" and "on" drug condition respectively; axial symptoms worsened significantly, as well as dysphagia and MMSE score; (ii) activity of daily living (UPDRS II) improved by 50% at the five-year follow-up but worsened progressively until reaching baseline ratings.

Conclusions: Some drug-resistant motor (postural instability) and non-motor (dysphagia and cognition) symptoms affect functional outcome of STN stimulation in the long-term follow-up.

3/OP43

IS AGE THE ONLY PREDICTOR OF POOR LONG-TERM FUNCTIONAL OUTCOME IN PARKINSON DISEASE AFTER STN STIMULATION?

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Objectives: to find predictive factors of functional recovery in PD at five-year follow-up and, particularly, to assess age role in motor and functional status post-DBS. **Methods:** Fifty consecutive PD patients were prospectively assessed yearly for 5 years after bilateral STN implant. Parkinsonian motor symptoms were evaluated with (on) and without (off) levodopa treatment, with and without bilateral stimulation. Disease-related disability (UPDRS-II score), neuropsychological and mood evolution were comprehensively studied. To assess age role we studied and compared outcome measure evolution separately in patients with <60-year old and those with >60-year old. A stepwise regression was applied in order to find predictors of UPDRS-II (ADL) score at the fifth follow-up (T5) among the following factors: age, response to L-DOPA challenge, UPDRSIII score in Off-med, MMSE score, FAB score.

Results: At five years follow-up, six patients died and two were lost to follow-up. In the remaining: (i) parkinsonian motor symptoms (UPDRS III) improved by STNs by 52% ("off" drug) and 68% ("on" drug) with respect to baseline pre-surgical "off" drug condition, axial symptoms worsening significantly; (ii) activity of daily living (UPDRS II) improved by 48%; (iii) the severity of levodopa-related motor complications was decreased by 70% and LEDD was reduced by 65%. Cognitive performance declined slightly (verbal fluency worsened significantly). Dysphagia, drooling, hypophonia and apathy emerged as newly referred symptoms in around 20% subjects.

Subjects over-60 showed worse gait performance, freezing, dysphagia and FAB score than younger patients. UPDRS-II and III scores at baseline and FAB score at 5-year follow-up predicted UPDRSII score at 5-year follow-up.

Conclusions: older patients showed faster evolution of axial and non motor symptoms than younger subjects at 5 years of chronic DBS. Age did not play a significant role towards functional outcome in the long term. Baseline motor impairment and executive functions were best predictors of ADL scale score.

TYPE OF ANAESTHESIA DOES NOT INFLUENCE THERAPEUTIC OUTCOME OF SUBTHALAMIC NUCLEUS DEEP BRAIN STIMULATION IN PARKINSON'S DISEASE

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Objective

To evaluate whether mode of anaesthesia impacts on efficacy of image-guided subthalamic nucleus (STN) deep brain stimulation (DBS) in Parkinson's disease (PD).

Methods

Motor scores of the Unified Parkinson's Disease Rating Scale (UPDRS-III) and surgical complications were compared between 14 patients (8 males, mean age 56.1 years, disease duration 13.8 years) operated under general anaesthesia (GA), and 68 patients (45 male, mean age 57.5 years, disease duration 15.2 years) under local anaesthesia (LA). In both groups, surgery was performed with MRI-based targeting of the visualized STN without microelectrode recording and with immediate postoperative stereotactic MRI. Mean follow up was 14 months.

Results

At baseline, UPDRS-III was worse in the GA than in the LA group, both on-medication (GA: 20.9±10.8; LA: 13.2±7.8, p<0.01) and off-medication (GA: 57.9±16.6; LA: 48.2±15.7, p<0.05). Motor scores on-stimulation off-medication significantly improved to 27.3±11.8 in the GA group and to 23.7±11.8 in the LA group. Percentage improvement was similar in both groups (GA: 52.8 %; LA: 50.8 %, p =n.s.). Transient surgical complications occurred in one patient (7.1 %) in the GA group (hallucinations) and seven patients (10.3 %) in the LA group (agitation in four, seizure, non-symptomatic subcortical bleeding and pulmonary embolus in one patient each).

Conclusions

MRI-guided STN DBS is as safe and effective under GA as LA, despite GA patients having significantly more severe baseline PD symptoms than those operated under LA.

5/OP45

COMPARISON OF ACCURACY OF 1 AND 3 TESLA STEREOTACTIC MRI-BASED TARGET COORDINATES IN DBS TARGETING

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Introduction

For DBS targeting surgeons employ MR imaging for pre-operative target selection.

MR distortion may cause target-selection error which contributes to error in electrode placement.

Reports on errors vary from 1.2 ± 0.6 mm to 3.2 ± 1.4 mm

No data in literature were found where accuracy of 1 Tesla and 3 Tesla MRI for DBS targeting was compared.

Aim of study

Comparison of target coordinates on 1T and 3T MRI and to define the potential difference in the accuracy of preoperative targeting on 1T and 3T MRI.

Material and methods

Six patients with different movement disorders (Parkinsons disease, essential tremor, and dystonia) were the subject of the prospective study.

In all cases the Medtronic Softwer given (Medtronic Stealth-Station, Treon Plus, Framelink 4), and also the manually adjusted or empirically calculated X, Y, Z coordinates of Gpi, Vim, and STN, plus the coordinates of fiducials, the anterior and posterior commissures were calculated, and also the intercomissural distance (ID) were measured on both 1T and 3T MRI using MPRAGE and T2 sequences.

The differences were measured, and statistically analysed by Manns-Whitney Test.

The frequencies of data were analysed according to the 50% percentiles.

Results

Statistical analysis showed no significant differences in the planning accuracy of target X,Y,Z coordinates, sides, commissures, or IC distances compared 1 Tesla to 3 Tesla.

However significant differences ($p < 0,009$) were found between 1 Tesla and 3 Tesla

in the accuracy of the fiducial coordinates. The accuracy was higher on 1 T (Median: 0,3550) compare to 3 T (Median: 0,8500).

Conclusion

On planning for DBS targeting no significant differences were found in TG coordinates between 1 Tesla and 3 Tesla MRI.

Only significant differences ($p < 0,009$) were found in the coordinates of the fiducials.

The accuracy was higher on 1 T (Median: 0,3550) compare to 3 T (Median: 0,8500).

According to results there was no significant impact on planning accuracy between 1T and 3 T in DBS targeting.

6/OP46

SUBTHALAMIC DEEP BRAIN STIMULATION IN PARKINSON'S DISEASE UNDER DIFFERENT ANESTHETIC MODALITY – A LONG-TERM COMPARATIVE COHORT STUDY

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BACKGROUND: In this long-term cohort study, we compare the outcome of PD patients who receive STN-DBS under general anesthesia (GA) and local anesthesia (LA).

METHODS: A consecutive of seventy-one PD patients with STN-DBS were enrolled into this study. Thirty-six patients were assigned as GA group, who received desflurane conditioned GA during bilateral STN electrode implantation. And 19 patients as LA group, with scalp regional anesthesia. Twenty-one patients were excluded from this study. The choice into either group was by patient's own preference. The micro-electrode recording was performed in both groups. The surgical outcomes were evaluated by UPDRS in at least 12 months after surgery.

RESULTS: The mean age at the time of surgery on both group GA/LA were 60.8 ± 9.1 and 53.8 ± 13.4 year-old respectively ($p = 0.026$). The mean follow-up duration were 32.4 ± 17.0 months (12 months to 71 months) and 26.2 ± 13.7 months (12 months to 61 months) respectively. Post-operatively, there had no significant different in the UPDRS Med OFF/DBS ON scores on both groups, except posture and gait, where GA group was improved by 1.19 ± 1.47 and LA group was improved by 2.16 ± 1.57 ($p = 0.0282$).

CONCLUSION: Conditioned GA was proved to be a good alternative anesthetic method for patients with PD who are unable to tolerate STN-DBS surgery while receiving a regional anesthesia. Their long-term motor outcomes were comparable.

7/OP47

DEEP BRAIN STIMULATION OF THE PEDUNCULOPONTINE TEGMENTAL NUCLEUS IN THE RAT 6-HYDROXYDOPAMINE PARKINSON MODEL: EFFECT ON C-FOS EXPRESSION

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Objectives: Deep brain stimulation (DBS) is used to alleviate motor dysfunction in Parkinson´s disease (PD). The pedunculopontine tegmental nucleus (PPTg) may be a potential target for severe postural instability with 25 Hz stimulation being considered more effective than 130 Hz stimulation. We here evaluated the expression of c-fos after 25 Hz and 130 Hz DBS of the PPTg in the rat 6-hydroxydopamine (6-OHDA) Parkinson model.

Methods: Anaesthetized male Sprague Dawley rats with unilateral 6-OHDA induced nigrostriatal lesions were stimulated with 25 Hz, 130 Hz, or 0 Hz sham-stimulation for four hours by electrodes implanted into the ipsilateral PPTg. Thereafter the distribution and number of neurons expressing the immediate early gene c-fos, a marker for acute neuronal activity, was assessed.

Results: DBS of the PPTg induced strong ipsilateral c-fos expression at the stimulation site, with 25 Hz having a more marked impact than 130 Hz. Additionally, c-fos was strongly expressed in the central gray. In the dorsal part of the central gray expression was stronger after 25 Hz stimulation, while in the medial and ventral part there was no difference between 25 Hz and 130 Hz stimulation. Expression in the basal ganglia was negligible.

Conclusions: In the rat 6-OHDA Parkinson model stimulation of the PPTg did not affect c-fos expression in the basal ganglia, but had a strong impact in other functional circuitries. PPTg stimulation might therefore interfere with other neuronal systems. Careful analysis of possible interferences with these systems in men is necessary.

8/OP48

INTRATHECAL BACLOFEN THERAPY FOR HARMFUL ADULT SPASTIC PATIENTS OF CEREBRAL ORIGIN

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Introduction:

Spasticity is a significant problem for many patients with central nerves system injury. Severe spasticity can impair mobility, hand skill, and independent functioning, as well as seating comfort. A significant number of patients with more severe or generalized spasticity, however, fail to improve or experience unacceptable side effects after conventional oral drug therapy. The use of intrathecal baclofen has been shown to be effective in reducing symptoms in patients with severe intractable spasticity, at concentrations of the drug of less than those of orally. However, most of the patients of ITB therapy were spinal origin or pediatric patients. Adult spastic patients of cerebral origin, for example, after stroke were not so many in previous reports.

Methods:

We report over the long-term follow up of 12 adult spastic patients of cerebral origin (7 cases after cerebral stroke, 3 cases after cerebral trauma and 2 cases after central nervous degeneration) were treated by continuous intrathcal administration of baclofen via a subcutaneously implanted pump.

Results:

A significant decrease in tone, spasm, function and QOL was observed in all patients without adversely affecting muscle strength of the unaffected limb. Efficacy remained stable after 6 months to over 2 years.

Conclusions:

Data suggest that ITB therapy is a safe and efficacious treatment for intractable harmful adult spastic patients of cerebral origin.

PSYCHOSURGERY

ORAL PRESENTATIONS

1/OR55

DEEP BRAIN STIMULATION IN OBSESSIVE COMPULSIVE DISORDER: DOUBLE-BLIND CROSSOVER STUDY

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Background Obsessive-compulsive disorder (OCD) is a chronic disease, in which up to 7% of patients remain severely affected and run a chronic deteriorating course when best medical treatment is applied. Deep brain stimulation has been applied in various surgical targets. Our objective was to determine whether bilateral deep brain stimulation of the nucleus accumbens is an effective and safe treatment for therapy-refractory OCD.

Methods The study consisted of an open eight month treatment phase, followed by a double-blind cross-over phase with randomly assigned two-week periods of active and sham stimulation, ending with an open twelve month maintenance phase. Sixteen patients (18-65 years) with OCD according to DSM-IV criteria, meeting stringent criteria for therapy-refractoriness, were included in the study. Primary efficacy was assessed by change from baseline on the Yale-Brown obsessive-compulsive scale (Y-BOCS).

Results In the open phase, the mean Y-BOCS score decreased by 46% from 33.7 ± 3.6 at baseline to 18.0 ± 10.1 ($p < 0.01$) after eight months. Nine out of 16 patients were responders with a mean Y-BOCS decrease of 23.7 ± 7.0 or 72%. In the sham-controlled phase, the mean difference between active and sham stimulation on the Y-BOCS was 8.8 ± 9.1 ($p < 0.01$) or 42%. Depression and anxiety decreased significantly. Except for mild subjective memory disturbances and word finding problems, no permanent adverse events were reported.

Conclusion The results of this study suggest that bilateral deep brain stimulation of the nucleus accumbens may be an effective and safe treatment for therapy-refractory OCD

2/OR56

3-D RECONSTRUCTION OF THE HUMAN NUCLEUS ACCUMBENS

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Introduction and Objectives: The human Nucleus Accumbens (NAc) plays an important role in several neuropsychiatric disorders and became a good target for their treatment by Deep Brain Stimulation (DBS). In previous works this group defined its stereotactic coordinates and limits. The study of the NAc 3-D stereotactic image reconstruction would improve such surgical procedures, namely by helping to define the best approach routes. It is the objective of the present study.

Method: 9 normal human adult NAc from both sexes were studied. Their histology was previously observed on serial coronal slices, stereotactically oriented and marked. The nucleus outline and the references were traced on the digitized images at each cutting level, allowing slice by slice 2-D individual variability analysis and then the reconstruction of the 3-D model (only including the posterior part of the NAc, where its limits are clear).

Results and Conclusions: The human NAc was visualized in both static and dynamic displays, enabling the evaluation of several features: it is a globose structure, lateral-dorsally flattened, with its main axis slightly descending laterally, almost entirely seated below the Anterior Commissure (AC). Its dimensions (mean values) are: height -7mm, width -14mm (larger on the right side), length (posterior part, until AC) -10mm.

The different view angles and perspectives are shown in the presentation.

DEEP BRAIN STIMULATION OF THE NUCLEUS ACCUMBENS CORE AND SHELL: LET'S MAKE IT WORSE.

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Introduction: The nucleus accumbens (NAc) is gaining interest as a target for deep brain stimulation (DBS) in refractory neuropsychiatric disorders with impulsivity as core symptom. The NAc is composed of two subterritories, core and shell, which have different anatomical connections. In animal models, it has been shown that DBS of the NAc changes impulsive action. Here, we tested the hypothesis that a change in impulsive action by DBS of the NAc is associated with changes in dopamine levels.

Methods: Rats received stimulating electrodes either in the NAc core or shell, and underwent behavioural testing in a reaction time task. In addition, in a second experiment, the effect of DBS of the NAc core and shell on extracellular dopamine and serotonin levels was assessed in the NAc and medial prefrontal cortex. Control subjects received sham surgery.

Results: We found that DBS of the NAc shell stimulation induced more impulsive action but less perseverative checking. These effects were associated with increased levels of dopamine and serotonin in the NAc, but not in the medial prefrontal cortex. DBS of the NAc core had no effect on impulsive action, but decreased perseverative responses indicative of a better impulse control. In these subjects, no effects were found on neurotransmitter levels.

Conclusions: DBS of the NAc shell has negative effects on impulsive action which is accompanied by increases of dopamine and serotonin levels in the NAc, whereas DBS of the NAc core has beneficial behavioural effects.

THE MEDIAL FOREBRAIN BUNDLE IN MAN: A FORGOTTEN STRUCTURE AND ITS ROLE IN THE CIRCUITRY OF DEPRESSION – AN ANALYSIS WITH DTI FIBER TRACKING

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Objectives: The purpose was to utilize DTI for the identification, presentation and description of an in man anatomically underdescribed fiber pathway, the medial forebrain bundle (MFB). In the second study, remote connectivity of historical lesioning targets for the treatment of major depression (MD) were scrutinized concerning distant fiber structures of overlap.

Methods: In the *anatomical study* a deterministic tracking procedure with individual single regions of interest were used (n=18) to identify and describe the MFB and the anterior thalamic radiation (ATR) as distinct fiber pathways. They were presented in the MNI152 space. In the *connectivity study* the four historical targets (AC,ACT,SCT,LL) for depression surgery were simulated (n=53). A probabilistic tracking procedure was used to investigate their connectivity. **Results:** The MFB and ATR were visualized as distinct, robust and separable structures for the first time. The MFB is bipartite, shows connections to the cerebellum and connects the VTA via a lower inferomedial branch to the lateral hypothalamus. A superolateral branch (slMFB) connects the VTA to the anterior limb of the internal capsule, nucleus accumbens and extends further into the frontal lobe. It runs antidromic to the known frontopontine tract (Arnold's bundle). Shared overlapping connectivities of historical lesion sites mapped on to the most mediobasal aspects of bilateral frontal lobe fibers were found. Access to these shared tracts may derive from the newly and here described and in man understudied slMFB.

Conclusion: The results might prove to have implication for the development of new target sites for DBS surgery in various disorders.

5/OR59

DEEP BRAIN STIMULATION OF THE NUCLEUS ACCUMBENS FOR THE TREATMENT OF ALCOHOL ADDICTION

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Objective: To investigate in pilot study the effect of N. accumbens (Nacc.) deep brain stimulation (DBS) on alcohol dependency.

Methods: Main inclusion criteria were history of alcoholism of at least 10 years and at least two long-term inpatient therapies plus unsuccessful medical treatment. We implanted brain electrodes (Medtronic, model 3387) bilaterally placing two distal contacts in the caudo-medial accumbens. Stereotactic coordinates were: 2mm rostral to the anterior border of AC, 3- 4 mm ventral, 6-8 mm lateral of the midline. Temporarily externalized electrodes enabled stimulation with different parameters and electrophysiological recordings during psychological tasks. Follow-up visits included extensive neuropsychological tests to document craving behavior, possible personality changes or cognitive impairment. Regular blood sampling enabled registration of serum markers indicating regular alcohol uptake.

Results: Seven patients were enrolled into the study to date. In one case infection required complete removal of the DBS-system 4 weeks after implantation. Nacc-DBS (130 Hz, 90 µsec, 4.5 V) gained complete response in 5/6 patients (no relapse, no alcohol uptake) and partial response in one case (occasional relapses but no craving) The median follow-up time was 21.3 months (range: 6-31 months). Neurophysiological results suggested that the NAcc is sensitive to alcohol-related cues and that the induction of craving is highly automatic.

Conclusions: There is preliminary clinical and neurophysiological evidence that bilateral high frequency Nacc-DBS has a long lasting suppressive effect on craving in patients with a long history of alcohol dependency, who were unable to abstain from drinking and experienced repeated relapses prior to the stimulation.

ORAL POSTERS

1/OP49

THE HUMAN NUCLEUS ACCUMBENS AS A TARGET FOR STEREOTACTIC NEUROSURGERY: A COMBINED MORPHOMETRIC STUDY

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Objectives: The human nucleus accumbens (NA) is the most prominent part of the ventral striatum covering a large area of the basal forebrain rostral to the anterior commissure. Stereotactic surgery of the human NA is a neurosurgical achievement of the 21st century. The purpose of our clinically oriented study was to provide anatomic and radiologic data of the human NA, primarily useful to neurosurgeons applying stereotactic surgery.

Methods: For our imaging study we used cerebral MRIs from 26 neurosurgical patients. The material of our anatomic study consisted of 32 cerebral hemispheres from 18 normal human brains. We localized the NA and measured and analyzed its dimensions (width, length, height and maximum diameter), at specific neurosurgically important levels (axial, coronal and sagittal).

Results: In axial MRI sections we found statistically significant difference of the mean value (MV) of the NA width as well as NA maximum diameter between individuals <60 and >60 years old ($p < 0.01$). We also found that individuals with putamen microcysts have a significantly greater MV of the NA maximum diameter. A statistically ambiguous difference of the MV of the NA length was found between males and females ($p < 0.1$), but this difference was statistically significant between individuals <60 and >60 years old ($p < 0.05$).

Conclusions: We present the largest morphometric study of the human NA (based on 84 nuclei), providing evidence of age-related morphometric changes. At the studied levels the NA has a wide enough surface ($>80\text{mm}^2$) for easy identification on preoperative and postoperative MRIs.

DEEP BRAIN STIMULATION IN LESCH-NYHAN DISEASE (LND): REPORT OF TWO CASES

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Objective: To investigate the effect of bilateral GPi stimulation for Lesch-Nyhan disease.

Background: The Lesch-Nyhan disease is a rare X-linked genetic and biochemical disorder caused by a complete deficiency in hypoxanthine-guanine phosphoribosyltransferase (HPRT). It is characterized by an overproduction of uric acid and by an abnormal behavioural phenotype with repetitive severe self-mutilations, mental retardation and general dystonia. The pharmacological treatments of LND has not been effective. Few patients have been subjected to DBS therapy shown initial good results for both dystonic and self-aggressiveness disorders.

Methods: Two patients (5- and 19-year old at the time of surgery) presenting dyskinesia, generalised dystonia and self-mutilating behaviour, were subject to bilateral implantation of DBS electrodes in the posterior area (motor) of GPi. In addition, in the second case the anterior/medial (limbic) area of Gpi was also target. Chronic DBS was applied using 130Hz; 450µs and 1.8 - 2.0 V.

Results: In both patients a markedly decreased aggressiveness was the first detectable change one week after surgery. A follow-up performed 44 and 28 month respectively showed a significant reduction in the self-mutilating behaviour and movement disorders. However, in the first patient the worsening of the effect late disruption of one electrode was associated with the recurrence of the preoperative symptoms.

Conclusions: The effectiveness of single or dual pallidal DBS for LND is not well established yet due to very few cases reported in the literature. The data provide more evidence that GPi stimulation is effective to treat self-aggressiveness and dystonia in LND.

3/OP51

BILATERAL STEREOTACTIC ANTERIOR CAPSULOTOMY FOR OBSESSIVE-COMPULSIVE DISORDER: LONG-TERM FOLLOW-UP.

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Severe Obsessive-compulsive disorder (OCD) that is non-responsive to pharmacotherapy or psychotherapy is a major psychiatric problem. Refractory cases to traditional treatments are often considered for surgery. One target of psychosurgery is the anterior limb of the internal capsule (AL-IC). Historically, ablation techniques were used to target the anterior limb. However, since the 1990s, Deep Brain Stimulation (DBS) is an alternative approach to this pathology, mostly because of its nonablative nature.

Recent studies are focusing on DBS of the anterior capsule; however long-term follow-up is not available. To acquire knowledge about this target and its lesion-effect on a long-term basis, we reviewed eighteen cases of anterior capsulotomy (AC) done in our center since 1994. This retrospective study will serve as a template to compare our results with our recent DBS-treated patients.

The technical aspect, the lesion size, the complications and the follow-up will be presented and discussed. We will also compare our results with the known literature on anterior capsulotomy, since this technique is still used in some countries for financial aspect.

4/OP52

SURGICAL TREATMENT OF MENTAL DISORDERS

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Objective: To evaluate the role of cingulotomy in treatment of mental disorders

Method: The author presents 19 cases with medically refractory mental illness underwent cingulotomy. The patient present with:

- Severe depression: 3 cases
- Aggressive syndrome: 3 cases
- Obsessive-compulsive disorder: 7 cases
- Schizophrenia with depression or aggressive as prominent symptom: 6 cases

The base of anatomy, Physiology, Indication and Technique were discussed.

Results: There are 14 men (73,7%) and 5 female (26.3%)

Evaluation of results was realized according to Pippard grade (1981)

- ▶ Amelioration: 14 cases (73,7%), grade II of Pippard.
- ▶ Partial Improvement: 3 cases (15,7%), grade III of Pippard.
- ▶ No improvement: 1 case (5,3%), grade IV of Pippard.
- ▶ Dead: 1 case (5,3%).

The following surgical complications were seen

Conclusion: The Surgical treatment appeared helpfulness in some cases of medical refractory mental Disorders. The longer follow-up is necessary.

Key words: mental disorders, cingulotomy , Schizophrenia

VAGUS NERVE STIMULATION IN TREATMENT-RESISTANT BIPOLAR DEPRESSION

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Objective: To evaluate four consecutive bipolar patients with treatment-resistant depression who completed 6 months of open-label Vagus Nerve Stimulation (VNS) therapy.

Materials and methods: Four patients (three females and one man; mean age 53.5 years) were evaluated with periodic monthly clinical evaluations before and after implant. The patients were evaluated with the following rate scales: HDRS, MADRS, HARS and weight changes. Also the side effects of VNS were recorded.

Results: The results are significant reduction between 30% and 40% of total scores compared to baseline scales and are consistent with literature data indicating a progressive symptom reduction from patients treated with VNS, with the most significant improvement in after the first 3 months of treatment. The patients needed a longer period of time to reach what is generally believed to be the lowest effective level of stimulation in terms of voltage (1mA).

Conclusions: The VNS exerts a positive effect not only over depressive symptoms but, also, on the cyclicity that characterizes various forms of mood disorders. The weight changes were a weight loss of 1.2 (± 1.2) kilograms after 6 months. The side effects at VNS start gradually subsided throughout 3 months.

6/OP54

DEEP BRAIN STIMULATION FOR TREATMENT-RESISTANT DEPRESSION. PILOT STUDY

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Objectives

Major depressive disorder has become an important health problem; 25 to 40 % of patients present a recurrence. Only two-thirds of depressive patients show a complete remission. Neurosurgery for psychiatric disorders has demonstrated a good response in patients with intractable affective and obsessive compulsive disorders.

Deep brain stimulation is a reversible, nonablative and modulatory procedure.

Several targets have been proposed as potential treatment for refractory depression, going from nucleus accumbens, subgenual cingulated cortex and inferior thalamic peduncle.

Methods

We realized a prospective study. This protocol was submitted to the ethics committee of our hospital and accepted. A committee for Neurosurgery for psychiatric disorders is part of our neurosurgery department and all the cases are discussed in a multidisciplinary team. Patients were diagnosed as treatment-resistant depression. 3 cases were selected and accepted.

Results

We present 3 cases with a follow-up more than a year; 3 females, from 40-65 years, more than 2 years in treatment for depression and no response. Deep brain stimulation of the right accumbens nucleus was performed.

Multiple Psychiatric Rating Scales for Depression were realized.

Conclusions

In this small case-series we present the results that were significant in all three patients and no complications for the procedure. Deep brain stimulation could be an effective and safe procedure for treatment-resistant depression.

PAIN II

ORAL PRESENTATIONS

1/OR60

TREATMENT OF INTRACTABLE CHRONIC CLUSTER HEADACHE BY OCCIPITAL NERVE STIMULATION: A PROSPECTIVE PILOT STUDY IN 8 PATIENTS

Fontaine Denys (Hopital pasteur Nice), Sol Jean Christophe (Hopital rangueil Toulouse), Fabre nelly (Hopital Rangueil Toulouse), Lanteri-Minet Michel (Hopital Pasteur Nice), Geraud Gilles (Hopital rangueil Toulouse)*

BACKGROUND : Chronic Cluster headache (CCH) is a form of primary headache that features repeated attacks of severe headache usually occurring several times a day. For these patients the medical options for therapy are often restricted. Occipital nerve stimulation (ONS) is a new, conservative and safe strategy recently reported for intractable CCH.

OBJECTIVE: To describe the clinical outcome of occipital nerve stimulation (ONS) for 8 patients with intractable chronic cluster headache.

METHODS: Eight patients with medically intractable CCH were implanted on the side on the side of the headache with unilateral electrodes in the suboccipital region for ONS. On a prospective assessment patients were asked to record details of frequency, intensity (EVA), WBPQ scale, and symptomatic treatment for their attacks in a diary before and after ONS.

RESULTS: At a median follow-up of 15 months (range 6-30 months) 6 of 8 patients reported improvement and recommended the treatment. Improvement occurred in both frequency and severity of attacks. No adverse events were noted.

CONCLUSION: Intractable chronic cluster headache is a disabling condition that has traditionally been treated with cranially invasive or neurally destructive procedures. ONS could be an efficient treatment and could offer a safe alternative option for some patients with CCH.

2/OR61

CHRONIC HYPOTHALAMIC DEEP BRAIN STIMULATION ALTERS BRAIN FUNCTIONAL CONNECTIVITY

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Introduction

High frequency Deep brain Stimulation (DBS) is thought to inhibit neuronal activity of the stimulated target. However evidence suggests that long-term stimulation results in more complex changes in neuronal networks and activity. Clinical effect of stimulation may be due to the stimulation driving plastic reorganization. We used pre-and-post-DBS neuroimaging techniques to investigate the chronic effects of high frequency hypothalamic stimulation using probabilistic tractography and topographic mapping in 2 patients with cluster headache (CH).

Methods

Diffusion weighted data was acquired using echo planar imaging preoperatively and 3 years post hypothalamic DBS. Data was acquired for matched control subjects. After correction of eddy current distortion, fitting of diffusion tensors, Bayesian estimation of diffusion parameters using Markov Chain Monte Carlo sampling was carried out. Probabilistic tractography was performed to characterize connectivity of hypothalamic and other pain networks preoperatively and post-DBS. Topographic mapping of hypothalamic connectivity with predefined cortical targets areas was used compute changes in dominant cortical connectivity patterns. Further voxelwise analysis of fractional anisotropy was performed using a tract based spatial statistics method.

Results

Altered FA of the white matter skeleton was demonstrated in CH preoperatively ($p < 0.001$). Increased hypothalamic connectivity was evident post-stimulation, including increased connectivity with the periaqueductal grey area (PAG) as well as the dorsal medulla ($p < 0.05$). Probabilistic tractography of the PAG and hypothalamus demonstrated altered cortical connectivity patterns post-stimulation, approaching a profile similar to control subjects. Topographic mapping demonstrated alterations in dominant target connectivity patterns post stimulation.

Conclusion

This study demonstrates a reorganization of hypothalamic and PAG connectivity with DBS therapy. Pathological connectivity of the hypothalamus and PAG was re-organized post-DBS, approaching a similar connectivity profile as healthy control subjects. These findings may help elucidate the mechanisms of DBS, suggesting neuroplasticity involving a reorganization of target connectivity long-term.

3/OR62

SPINAL SEROTONERGIC RECEPTORS SUBSERVING DESCENDING PAIN CONTROLLING PATHWAYS ACTIVATED BY SPINAL CORD STIMULATION

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Background: Spinal cord stimulation (SCS) is since long extensively employed in the management of neuropathic pain but the underlying mechanisms is only partially understood. In a recent study performed on a rat SCS model, we demonstrated that the pain relieving effect appears to involve the spinal serotonin system.

Objectives: The present study aimed at identifying the subtypes of the spinal serotonin receptors_{1-4,6,7} by which the pain relief is mediated.

Methods: Experiments were performed on rats with neuropathy produced by partial ligation of the sciatic nerve. Tactile sensitivity was assessed using von Frey filaments, and cold and heat sensitivity with cold spray and radiant heat, respectively. Selective 5-HT subtype receptor antagonists (Methiothepin (5-HT₁, 5-HT₆, 5-HT₇), Ketanserin tartrate (5-HT_{2A}), TICM (5-HT₃), SDZ-205,557 (5-HT₄)), and 5-HT subtype receptor agonists (α -m-5-HT (5-HT₂), *m*-CPBG (5-HT₃)), or vehicle, were administrated intrathecally 5 min prior to the application of 30 min of SCS.

Results: Ketanserin and SDZ-205,557 significantly attenuated the suppressive effect of SCS on tactile hypersensitivity, while Methiothepin and TICM were ineffective. The suppressive effect on cold hypersensitivity of SCS was counteracted by Ketanserin only. None of the 5-HT subtype receptor antagonists attenuated the suppressive effect on heat hyperalgesia of SCS. The agonists α -m-5-HT and *m*-CPBG dramatically enhanced the suppressive effect of SCS on tactile hypersensitivity.

Conclusions: These results suggest that the activation of the 5-HT_{2A}, 5-HT₃ and 5-HT₄ receptors plays an important role in SCS-induced relief of neuropathic pain. The SCS effect on heat hyperalgesia appears to be independent of serotonergic mechanisms.

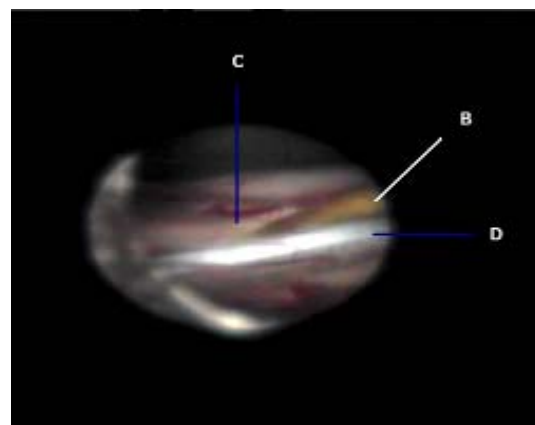
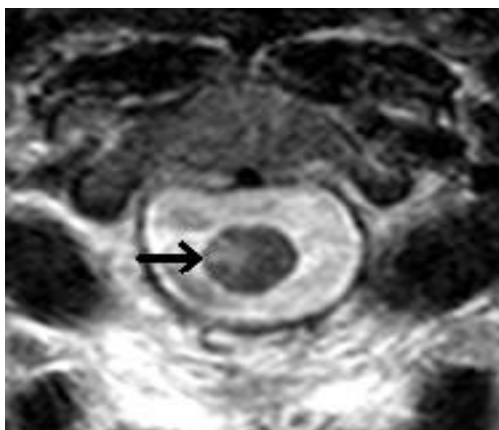
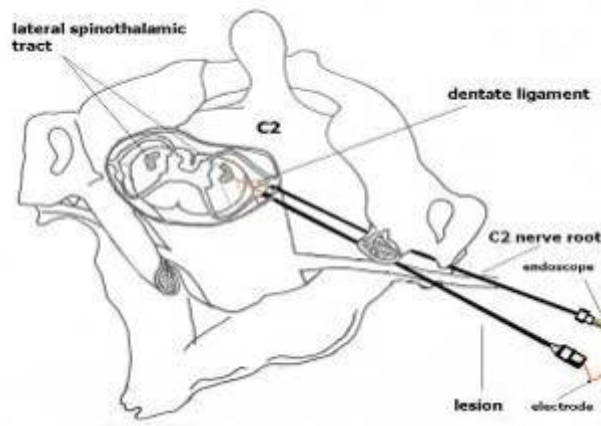
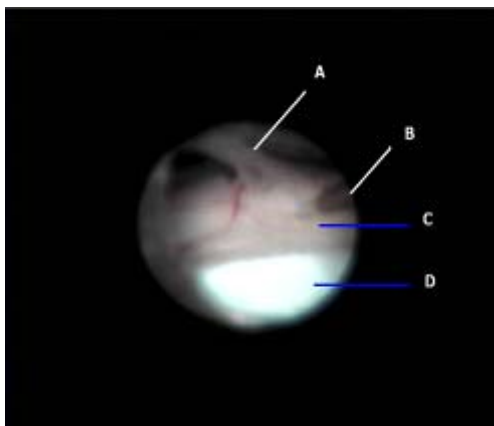
ENDOSCOPIC-GUIDED PERCUTANEOUS RADIOFREQUENCY CORDOTOMY : A NEW TECHNIQUE

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The authors present the first clinical implementation of an endoscopic assisted percutaneous anterolateral radiofrequency (RF) cordotomy. The aim of is to demonstrate the intradural endoscopic visualization of cervical spinal cord (SC) through percutaneous approach to refine the spinal target for anterolateral cordotomy, avoiding undesired trauma to the spinal tissue or injury to blood vessels. Initially, a lateral puncture of the spinal canal in C1-C2 interspace guided by fluoroscopy is performed. As soon as cerebrospinal fluid (CSF) comes out of the guide cannula (17 gauge needle), the endoscopic can be inserted for visualization of SC and its vicinities. The endoscopic visualization provided clear identification of the pial surface of SC, arachnoid membrane, dentate ligament, dorsal and ventral root entry zone and blood vessels. The target for electrode insertion into the SC was determined half distance from the dentate ligament and the ventral root entry zone. The endoscopic guidance shortened the fluoroscopy usage time and no intrathecal contrast was needed. Cordotomy was performed by standard radiofrequency method after the neurophysiological target refining. Satisfactory analgesia was provided by the procedure with no additional complications or CSF leak. The Initial use of this technique (20 patients) suggests that percutaneous endoscopic procedure may be useful for particular manipulation of the SC possibly adding safety to the procedures and improving its effectiveness.



5/OR64

PRE OPERATIVE MRI/MRA FOR MICROVASCULAR DECOMPRESSION IN TRIGEMINAL NEURALGIA. CONSECUTIVE SERIES OF 67 PATIENTS

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Background: Microvascular Decompression (MVD) is an accepted treatment for primary trigeminal neuralgia (TN). In recent years, efforts have been made to investigate the role of pre-operative MRI in selecting patients with neurovascular compression.

Methods: 92 consecutive patients underwent a standard retrosigmoid craniotomy for MVD between 2005 and 2009, of whom 67 had a pre-operative MRI and MRA according to the protocol of our Department. Operative findings were accurately recorded and compared to MRI results. Follow-up was in the form of telephone interview.

Results: Pre-op MRI sensitivity was 96%, while specificity was 67% (1 false positive among 3 patients with negative intra-operative findings). The predictive value of a positive MRI was 98%, while the predictive value of a negative MRI was 50%. At a mean follow up of 3.8 years (range 1-5) 55% of patients were pain-free, 22% improved and 22% showed modest or no improvement. There was a trend for patients with a negative MRI to have a poorer outcome compared to patients with a positive MRI, but the difference was not statistically significant (P= 0.059).

Conclusions: Pre-op MRI has both good sensitivity and positive predictive value. Specificity and negative predictive value were limited in this series. Both radiological and clinical criteria are important for patient selection.

6/OR65

OUTCOME OF 136 PERCUTANEOUS BALLOON RHIZOTOMY PROCEDURES FOR TRIGEMINAL NEURALGIA

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Objectives

Percutaneous balloon rhizotomy has been used to treat trigeminal neuralgia (TN) since the 1970s. Few large series have been reported. Therefore, we examined the efficacy and durability of the procedure as well as the predictors associated with earlier recurrence.

Methods

All patients undergoing evaluation for facial pain were entered into a prospective database. Data collected included the side, site and character of the pain, history of multiple sclerosis (MS), and details of previous procedures performed for TN. Data were analyzed using actuarial methods to determine the efficacy and durability of the procedure, as well as predictors of recurrence over time.

Results

Between May-01 and Mar-09, 90 patients underwent a total of 136 balloon compressions for TN (n=29 procedures for MS). 131 procedures (96.3%) resulted in improvement of pain at 3 months postoperatively. Of these, 107 were pain-free off all medication, and a further 5 patients were pain-free on some medication for an 82.4% chance of being pain-free. There were no serious adverse effects.

Analysis using a Cox proportional hazards survival model was performed. The presence of MS (HR=2.0 p=0.014) and pain described as 'always present' (HR=2.0 p=0.008) were associated with earlier recurrence. Median time to recurrence was 25 months in those with MS versus 40 months in those without.

Conclusions

Balloon compression was effective in achieving freedom from TN pain with minimal side effects. Pain which was 'always present' preoperatively or due to MS was associated with poorer long term outcomes.

7/OR66

BALLOON COMPRESSION FOR TRIGEMINAL NEURALGIA (TGN) - LONG TERM FOLLOW-UP: A SINGLE CENTRE EXPERIENCE.

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The Walton Centre for Neurology and Neurosurgery

OBJECTIVE

To look at the efficacy of balloon compression for TGN in a series of 104 consecutive patients operated in the Walton Centre for Neurology and Neurosurgery.

METHODS

Retrospective analysis of case files of patients with TGN over a period of 10 years (1999-2009) in relation to presentation, age, sex, co-morbidities, type of neuralgia, distribution, medical treatment, duration of pain relief, MRTA findings, complications and follow up.

RESULTS

A total of 104 patients with a mean age of 70.8 years (range 38-92) were included in the study. The female to male ratio was 1.4:1 (21% had multiple sclerosis). In 62.5% the neuralgia was on the right side. 13% had atypical presentation. Most common division involved was V2/V3 (43.2%). The follow up period was 9 yrs - 6 months, all patients except two had short term pain relief, pain relief at follow-up varied between 9 years to 1 month (mean 15 months). 48% had the procedure repeated due to pain recurrence. Side effect included numbness (59), corneal sensation (2 cases) and anaesthesia dolorosa (1 case).

CONCLUSION

The balloon compression for TGN is a safe procedure across the age group with a low complication rate. Repeat balloon rhizotomy are safe and not associated with higher morbidity rate. We did not find any difference between typical and atypical TGN, pain relief duration was longer for V2 and V3 TGN and in patients with multiple sclerosis.

8/OR67

SPECIFY 5-6-5 ELECTRODE FOR TREATMENT OF FAILED BACK SYNDROME: EXPERIENCE IN 21 CASES.

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Introduction

The Specify 5-6-5 electrode (Medtronic) is a surgical electrode that can be used for treatment of failed back syndrome. This is a prospective study of 21 patients in whom we examined pain relief and paresthesia coverage of the lower back and the lower limbs. Also feasibility of the minimal invasive implantation technique and awake testing is examined.

Material an Methods

Using a unilateral minimal invasive implantation technique with spinal anesthesia and peroperative awake paresthesia testing, we implanted the electrode as a first choice in 21 patients, 11 females and 10 males. They all suffered failed back syndrome with lower back pain and neuropathic pain in at least one leg. Pain relief, paresthesia coverage ,patient satisfaction and quality of life were examined.

Results

In 21 patients a Specify 5-6-5 electrode was implanted and after a trial period of 4 weeks, 19 patients received a definitive implantation with a Prime Advanced battery (Medtronic). There is a mean follow up of 11 months. For 11 of these patients we have a mean follow up of 14 months. All 19 patients have at present more than 50% pain relief. Lower back stimulation is present in 15 out of 19 patients. In the group with more than one year follow up this is present in 9 of 11 patients.

Conclusion

The Specify 5-6-5 electrode is easy to implant in a minimal invasive way with awake testing using spinal anesthesia. Programming possibilities are numerous and together with the electrodes' design this makes it more easy to continue to give pain relief more than 50% to the lower back region and the lower limbs together.

EPIDURAL ELECTRICAL AUDITORY CORTEX STIMULATION IN THE MANAGEMENT OF CHRONIC UNILATERAL DISABLING TINNITUS. FIRST RESULTS OF THE PILOT STUDY « ELECTIN ».

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INTRODUCTION

Subjective tinnitus can be very disabling when chronic. The pathophysiological basis for chronic tinnitus could be due to an aberrant cortical reorganization following a peripheral auditory deafferentation. The pilot study "ElecTIN" was designed to evaluate the effectiveness and the practical feasibility of epidural electrical auditory cortex stimulation (EEACS) on tinnitus.

MATERIAL AND METHODS

Two patients with unilateral chronic tinnitus have already benefited from this protocol. First, an active or sham rTMS was applied, then we proceeded to the EEACS. Finally, a randomized double-blind controlled assessment with a cross-over was done.

RESULTS

After rTMS sessions, no significant change was found in subjective intensity of tinnitus (VAS) or in multidimensional questionnaire. Both patients were implanted, using a neuronavigation system and intraoperative electrophysiological recordings of auditory cortical responses, for the positioning of electrodes.

In the first patient, an efficacy of EEACS was found during the open-period, with a 30% decrease of the VAS and an improvement of all scores on questionnaire.

For the second patient, the EEACS had a 70% efficiency on VAS. Due to a scar problem, the EEACS system had to be removed with a rebound effect on tinnitus intensity. Eighteen months later, the EEACS was re-implanted with an efficiency of over 50% on VAS of the intensity of tinnitus in active stimulation.

CONCLUSION

It is the first description of a re-implantation in the EEACS for tinnitus. Obtaining a similar efficacy in both procedure and a return to baseline during the interval without stimulation are important arguments in favor of the real effectiveness of EEACS.

ORAL POSTERS

1/OP55

SUBCUTANEOUS ELECTRIC STIMULATION FOR THE TREATMENT OF REFRACTORY PAIN OF DIFFERENT ORIGIN

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Subcutaneous electric stimulation has been recently reported to be effective in the treatment of pain from different origin and refractory to any drug or epidural stimulation therapy. 6 patients have been submitted to implant of a dual octopolar electrode (Boston Inc. USA) connected to a rechargeable stimulator (Boston Precision). 1 patient was affected by postherpetic trigeminal neuralgia at the first and second left branch, 1 patient was affected by pain at the median lumbar region due to failed back surgery syndrome, 1 patient was affected by hemithoracic pain due to surgical thoracotomy for cancer, 1 patient was affected by bilateral mandibular pain due to locoregional radiotherapy for throat and tongue cancer, 1 patient was affected by lumbar posterolateral postherpetic syndrome. 1 patient was affected by dorsal median pain due to repetitive surgeries of that region.

All patients were assessed and their pain was scored with VAS scale and their neuropsychological profile was traced. Patients with depression were withdrawn by this initial experience.

All the patients were submitted to a 40 minutes surgery under general anaesthesia.

The follow-up of these patients ranged from 5 to 9 months and pain was reduced from a mean VAS value of 8 to a mean VAS value of 3 shortly after implant and activation of the stimulator.

The different causes of pain in these patients suggest a possible wide range of applications of this kind of subcutaneous stimulation in treating painful patient through a simple surgical procedure.

2/OP56

SPINAL CORD STIMULATION FOR PAIN SECONDARY TO CHRONIC PANCREATITIS

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Background: Neuropathic visceral pain is a complication of chronic pancreatitis. The condition is usually difficult to treat, as it responds poorly to common analgesics and celiac plexus block. Two cases have been reported in the literature regarding the use of spinal cord stimulation (SCS) for relief of chronic pancreatitis-related pain.

Patients and methods: Two patients, aged 50 and 39, presented with intractable visceral pain related to non-alcohol related pancreatitis (1st patient) and alcohol-related pancreatitis (2nd patient). Both had a history of partial pancreatectomy and were taking high dose of opioids with no significant pain relief. A quadripolar electrode for SCS (Medtronic, model 3888) was inserted at the level of T8-T10 level using a percutaneous technique. After a 7 day trial, a permanent stimulator was inserted.

Results: At a mean follow-up of 7 years, both patients showed a marked improvement, with 80% and 90% decrease of pain respectively, as assessed by visual analogue scale. Pain medications were discontinued in both cases. No surgical complications were observed.

Conclusions: SCS appears to be an effective long-term treatment for neuropathic visceral pain related to chronic pancreatitis. More experience is needed to further validate this indication.

3/OP57

SPINAL CORD STIMULATION (SCS), AND/OR PERIPHERAL SUBCUTANEOUS FIELD STIMULATION (PSFS) IN THE TREATMENT OF DRUG-RESISTANT CHRONIC PAIN. A SINGLE CENTER EXPERIENCE OF 72 PATIENTS.

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OBJECTIVE

To evaluate the use of SCS and/or PSFS on the alleviation of treatment-refractory chronic pain.

PATIENTS AND METHODS

During the period 2006-2009, 72 patients with a history of drug-resistant chronic pain were subjected to trial implantation of electrodes for SCS (n=7), PSFS (n=28) or both (n=37). Failed back surgery (n=44), cervical myelopathy (n=7) trauma (n=3) and spinal tumors (n=5) were the most common underlying pathologies. In all cases, trial stimulation period lasted for 5 days, starting from the first post-implantation day.

RESULTS

Trial stimulation was positive (pain relief >50% in VAS scale) in 44 patients (61%). Chronic electrodes were implanted on 40 patients as follows: SCS 1, PSFS 11, and combined SCS/PSFS on 28 patients. All patients reported a sustained relief of pain. During follow up (which ranges from 6 months to 4 years), two postoperative infections and two hardware-related failures developed.

CONCLUSION

SCS and PSFS, applied as a single or combined treatment, can offer significant improvement in patients with chronic refractory debilitating pain, while carrying low complication rates. In our experience, proper patient selection is of fundamental importance for the success of the operation and the overall favorable outcome.

THE APPLICATION OF PULSED RADIO FREQUENCY IN CHRONIC PAIN

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Introduction:

In the last 25 years, neuromodulative techniques, such as spinal cord stimulation (SCS) or the intrathecal application of opioids, have replaced the old ablative neurosurgical methods.

The application of pulsed radio frequency (PRF) represents another addition to the arsenal of non-ablative techniques

Methods:

50 Patients with chronic, non-maligne pain, who underwent a PRF treatment using the PASHA Multi-Cath Electrode, from Jan. 2005 - July 2007, were included in this study. The major part, namely 19% suffered from FBSS (Failed Back Surgery Syndrome), while other diagnosis included spinal stenosis, degenerative processes, facette syndrome, trigeminous neuropathia and others.

The patients were treated with various stimulation parameters, including duration and number of pulses. After lumbar puncture, the electrode is placed epidurally, at the dorsolateral region of the spinal column, right above the dorsal root entry zone.

The dorsal roots are then stimulated, until noticed by the patient. Very low voltages (< 0.8V) are used, in order to ensure the best possible proximity to the nerve root.

Results:

Results were assessed, using a questionnaire, which included the severity of pain (using the visual analogue scale (VAS)), pain reduction, reduction of pain medication, as well as various parameters, which contribute to the patients' quality of life, such as overall activity, mood, mobility, the ability to work, sleep and vitality. The latter variables were used to determine a mean value, which represented quality of life.

Follow-ups were conducted after four weeks, 3, 6, 12 and 18 months respectively. The results show, that half the patients experienced a significant pain reduction of up to 61%, in comparison to their initial pain severity, which lasted for about six months. Thirteen patients remained after 18 months, displaying a mean pain reduction of 78%, the other patients dropped out, mainly due to recurring pain.

Conclusion:

The application of PRF to the spinal roots can be considered as a viable first-line, minimal invasive method, which can be easily repeated and has next to no side effects. The ability to conduct an SCS trial, as well as to apply a test-bolus of opioids in addition to the application of PRF, make the PASHA-Cath Electrode the perfect tool for determining the best course of action in the invasive treatment of chronic pain.

5/OP59

THE IMPORTANCE OF AUTONOMIC SYMPTOMS IN TRIGEMINAL NEURALGIA

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Introduction: Autonomic symptoms can occur in association with facial pain in trigeminal neuralgia (TN). The distinction between first division (V1) TN and trigeminal autonomic cephalgias, particularly Short-lasting Unilateral Neuralgiform headache with Conjunctival injection and Tearing (SUNCT) can be difficult.

Objective: To investigate the frequency of autonomic symptoms with TN and determine if their presence has any bearing on surgical outcome.

Methods: We reviewed 92 patients who had surgical procedures for TN, noting the pre- and post-operative visual analogue scores (VAS) and the presence of autonomic symptoms.

Results: 67% patients had at least one autonomic symptom associated with their pain.

In the 64 patients who had a microvascular decompression (MVD), 23 patients had no autonomic symptoms. Their mean pre-operative VAS was 9.55 and dropped to 0.3 at one year post-operatively. In the remaining 41 patients with associated autonomic symptoms, the mean pre-operative VAS was 9.2 and at one year post-operatively was 1.6.

At one year post-operatively, 11 of 41 patients with pre-operative autonomic symptoms had pain but in those without autonomic symptoms only 1 patient of 23 had pain ($p < 0.05$).

Conclusion: The presence of autonomic symptoms in TN significantly reduces the likelihood of being pain free after MVD. Neurosurgeons should be aware of SUNCT, especially in patients with V1 TN and autonomic symptoms, to ensure that all potential medical therapies have been tried prior to surgical treatment.

6/OP60

MASSETER MUSCLE WEAKNESS AFTER TRIGEMINAL GANGLION BALLOON COMPRESSION

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Objective:

The purpose of the present study is to assess the frequency and the severity of masseter muscle weakness, after percutaneous balloon compression (PBC) of the trigeminal ganglion, in patients suffering from trigeminal neuralgia (TN).

Methods:

Ten patients (7 males, 3 females), with idiopathic trigeminal neuralgia and mean age 69.2 ± 1.6 years, were enrolled in this study. All subjects underwent compression of trigeminal ganglion by balloon inflation, lasting 2,5-5 minutes. All patients went through, before, 1, 6 and 12 months after unilateral PBC, needle electromyography of masseter muscle and record of motor evoked potentials (MEPs), evoked by contralateral and ipsilateral transcranial magnetic stimulation (TMS).

Results:

The interference pattern at maximal effort was normal before PBC, 0-20% of normal in 6 patients and 50-80% in 4 patients 1 month post PBC, 60-80% in 7 and 100% in 3 patients 6 months post PBC and 100% in all ten patients 12 months post PBC. The mean MEPs' latencies, to contralateral and ipsilateral stimulation, were considerably prolonged 1 month after PBC (ANOVA test, $p = 0.022$ and $p = 0.059$ respectively), but normal values were noticed at the 12-month post PBC study.

Conclusions:

Masseter muscle weakness, after PBC of trigeminal ganglion, is probably due to a neurapraxic/demyelination process and it should be expected in all cases, but it appears to be reversible over a period of 6-12 months. Concerning bilateral pain, EMG and MEPs might be useful before contralateral PBC, which should be avoided for at least 6 months after the first operation.

7/OP61

CT- GUIDED BİLATERAL SELECTİVE PERCUTANEUS HİGH CERVİCAL CORDOTOMY İN CANCER PAİN

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Cancer pain resistant to medical treatment is an important issue in patients suffering from malignant diseases.

In this study, malignancies, locatization of pain, resolution of pain following the procedures, complications, follow-up results, their spinal cord diameters and skin dura distances of patients who underwent CT guided bilateral selective percutaneous high cervical cordotomy were analyzed.

Forty-four CT- guided uni- or bilateral selective percutaneous high cervical cordotomy operations were performed on 38 patients (28 male, 10 female) cancer pain resistant to medical treatment during September 2004-March 2010. The ages of the patients were 21-70 years. Thirty-two patients underwent the operation only once while 2 cases underwent the operation twice. Four of the patients underwent bilateral procedure. The causes of their malignancies were lung cancer (n:15), pancoast tumor (n:5), mesothelima (n:4), prostat cancer (n:2), vulva cancer (n:2) and others in 5 patients. Thirty five of the patients had arm, shoulder, and/or trunk pain while nine had leg pain. Mean VAS scores were 9.6. Total resolution of pain was seen in 39 of the cases (88.6%) while there was partial pain resolution in 5 of the cases. One of the patients experienced difficulty during urination as complication after the procedures.

Mean A-P and transverse diameters of the spinal cord at C1-2 level were calculated as 0.9 ± 0.18 mm and 1.1 ± 0.3 mm respectively.

CT- guided selective percutaneous high cervical cordotomy performed by experienced neurosurgeons in this field is a cheap, repetative and safe way of treatment for cancer pain resistant to pharmacotherapy.

OUR EXPERIENCE WITH PERCUTANEOUS RETROGASSERIAN GLYCEROL RHIZOTOMY FOR TREATMENT OF TRIGEMINAL NEURALGIA

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PURPOSE: We have evaluated the long-term results after percutaneous retrogasserian glycerol rhizotomy in our patients with trigeminal neuralgia.

MATERIALS AND METHODS: From August 1981 to July 1998 a total of 1683 percutaneous retrogasserian glycerol rhizotomies after Håkanson were performed. All patients were considered medical failures prior to the procedure. Using the Härtel approach, the intervention was performed with X-ray monitoring under local anaesthesia and rarely last longer than 30 minutes.

RESULTS: It achieved good results in the treatment of idiopathic trigeminal neuralgia (IT) and symptomatic trigeminal neuralgia due to multiple sclerosis (STMS): 94,0% of the IT-patients and 91,8% of the STMS-patients were completely free of pain after the intervention. Follow-up examinations up to 5 years and evaluation with special EDP-programs have made an individual and chronological comparison of the specific neurological status. This analysis has yielded a relapse rate of 25,9% in IT and 47,5% in STMS. Immediately postoperatively were found herpetic eruptions in 43,2% of cases. They occurred on the 3rd postoperative day and persisted for 2-3 weeks before being relieved by local virostatic therapy. Transient decreases in sensation (hypoesthesia/hypalgesia) occurred in 52,0% of the patients, but declined to 25,5% in the course of the observation period.

CONCLUSION: We believe that the Håkanson technique is safe, and effective in treating trigeminal neuralgia. In spite of high incidence of recurrence and of long-lasting dysaesthesias it is, in our opinion, the method of choice in the elderly, and high risk patients.

NAVIGATION – IMAGING - INSTRUMENTATION

ORAL PRESENTATIONS

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AWIGS - ADVANCED WORKSPACE FOR IMAGE GUIDED SURGERY – THE PERFECT TOOL OF INTRAOPERATIVE COMPUTED TOMOGRAPHY IN STEREOTAXY

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Introduction

Intraoperative computed tomography is a useful instrument for accurate image guided surgery. It is one of the main diagnostic instruments for stereotactic neurosurgeons because of its geometrical accurateness. Therefore the intraoperative use provides a lot of additional information compared to stereotactic x-ray devices. Highly accurate the position of electrodes can be documented and the content on information about soft tissue is far beyond of stereotactic x-ray devices.

We present our experience with an operation unit which combines a full functional operation table with a high resolution computed tomographic scanner.

Materials and Methods

In December 2001 the Advanced Workplace For Image Guided Surgery (AWIGS, Maquet, Rastatt, Germany) was for the first time nationally and internationally installed in the department of neurosurgery in Innsbruck. It consists of an operation table which is connected by rails with a computed tomograph (CT) HiSpeed X/I Z computed tomographic (CT) scanner (GE Medical Systems). From February 2002 until now more than 7000 patients were treated in that operating room. The intraoperative CT was used more than 1400 times in stereotactic operations. The AWIGS system provides the possibility of intraoperative CT images of high quality and reduces operation time of stereotactic operations without the necessity of reposition of the patient. The whole system is computer driven. In combination with the stereotactic planning device Precis Plus (Inomed, Tenningen, Germany) image fusion with MRI enables maximum information on the patients brain.

Results

The main purpose for the use of a intraoperative CT was a simplification of stereotactic imaging including gaining more information on our patients brain. The time saving according to the procedure with mounting the stereotactic frame to the head of the patient and transfer of the patient to radiology and transfer back to the OR is in minimum half an hour. Furthermore the patient needs not to be repositioned. Additionally subsequent postoperative controls are made before removing the stereotactic frame. That allows not only the early detection of complications like bleedings but gives immediately an accurate control of the surgery.

Conclusions

AWIGS is a powerful tool for planning as well as control of stereotactic operations. The AWIGS system improves stereotactic surgery dramatically. Stereotactic x-ray devices are history.

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BRAIN SURGERY IN A STEREOSCOPIC VIRTUAL REALITY ENVIRONMENT: A SINGLE INSTITUTION'S EXPERIENCE ON ONE-HUNDRED CASES

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Object: Assessing our clinical experiences using a novel approach - stereoscopic virtual reality environment (SVRE) – in order to help neurosurgeons with both surgical training and surgical strategic planning purposes.

Methods: Patient-specific Digital Imaging data that has been obtained from a variety of different diagnostic sources (CT, CTA, MR, fMR, MR-DTI) were collected and then transferred to a workstation (Dextroscope; Volume Interactions Pte. Ltd., Singapore) setting. These clinical data were obtained from 100 patients who were suffering from either brain vascular malformations or tumors that were located in difficult brain sites. A three-dimensional (3D) volume rendering was then produced for each of the 100 clinical cases, which were then subjected to data co-registration and fusion.

Results: By using different head positioning systems and craniotomy options, we simulated microscopic visualizations of the lesion through numerous surgical approaches and from various angles of view. This simulation strategy enabled us to carry out an approach selection and, eventually, to identify the optimum angle of lesion visualization.

Conclusion: These virtual craniotomies successfully simulated a sampling of different operative environments which, we believe, have the potential to play a significant role in neurosurgical training and operative planning worthy of further exploration and development.

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A SYSTEM FOR OPTICAL GUIDANCE DURING STEREOTACTIC NEUROSURGERY

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Introduction

Intracerebral measurements are necessary for target guidance and trajectory verification during deep brain stimulation (DBS) implantation. The aim is to develop a fast and easy-to-use optical intracerebral navigation technique for stereotactic DBS implantation.

Methods

Laser Doppler perfusion monitoring (LDPM) and reflectance spectroscopy are the optical core techniques used. A probe with four adjacent optical fibres and dimensions adapted to the Leksell Stereotactic System is used to create paths for the DBS electrode along the pre-calculated trajectory. The reflected light intensity at 780 nm is presented as a real-time curve representing grey-white tissue boundaries passed during the insertion. With the probe connected to the LDPM system the microvascular perfusion can be presented as well.

Results

The system has been used successfully in more than 70 DBS-implantation procedures. A measurement is finalized within minutes and with a resolution better than 1mm. When comparing with preoperative MRI the reflected light intensity can be used to verify the planned trajectory. Characteristic curve forms towards the subthalamic nucleus and the globus pallidus internus (GPI) have been identified. The curves start with a low intensity in cortex and increases to a maximum value in subcortical white matter and drops to an intermediate level characteristic for the target aimed at. As white matter has a slightly shorter "look ahead distance" than grey matter it is possible to identify the lamina surrounding the GPI.

Conclusion

Real-time presentation of grey-white tissue boundaries during DBS implantation can be achieved within minutes by means of LDPM and reflectance spectroscopy.

QUANTITATIVE FLUORESCENCE AS A DIAGNOSTIC BIOMARKER FOR INTRACRANIAL TUMOR: IMPLICATIONS FOR LOW GRADE GLIOMA SURGERY

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Objective: Intraoperative, in vivo quantitative fluorescence, induced using orally administered 5-ALA, was investigated across a variety of intracranial tumors to assess its diagnostic efficiency relative to conventional qualitative fluorescence.

Methods: A fiber-optic probe connected to a spectrometer interrogated multiple spatially co-registered sites during 15 resective procedures, including 2 low grade gliomas, 3 high grade gliomas, 7 meningiomas, and 3 metastatic tumors from lung. A light transport modeling technique was used to derive absolute protoporphyrin IX concentrations. A receiver operating characteristic (ROC) analysis was then performed to assess diagnostic efficiency, and this was compared with that for qualitative visible fluorescence.

Results: Absolute protoporphyrin IX concentrations were statistically elevated in all tumor types, despite many falling below the threshold of visual detection. The light transport model far exceeded the distinguishing abilities of previously reported raw spectrographic signatures. ROC area-under-the-curve analysis demonstrated an optimal classification efficiency of 87% for the set of all tumors (versus 66% for conventional qualitative fluorescence), with a specificity of 92%, sensitivity of 84%, positive predictive value of 95%, and negative predictive value of 77%. Classification efficiency was 76% for low grade gliomas, 93% for high grade gliomas, 97% for meningiomas, and 95% for metastases.

Conclusions: Quantitative fluorescence reveals significantly elevated concentrations of the fluorophore protoporphyrin IX across multiple intracranial tumor types, including low grade gliomas, suggesting substantially greater potential utility of this biomarker in tumor resection.

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USE OF A FRAMELESS NEURONAVIGATION SYSTEM (NEXFRAME) IN DEEP BRAIN STIMULATION

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OBJECTIVES

Stereotactic systems are traditionally used in order to get the right target in deep brain stimulation (DBS). Recently, the use of the 3 tesla MRI has enabled us to recognize directly the targets and consequently, the elaboration of these images on the neuronavigator allowed us placing the electrode using a frameless technique (Nexframe, Medtronic) in spite of the traditional frame.

Compare with frame, we evaluate the advantages and reliability of the frameless technique.

MATERIALS AND METHODS

We present a series of 15 patients operated since January 2010. 7 dystonic patients and 8 parkinsonian patients (9 male, 6 female; age between 17 and 62 years). Surgical planning has been done through 3T-MRI fused with axial tomography. The targets were subthalamic nucleus (STN) for Parkinson's disease and ventroposterolateral part of internal pallidum (GPI-VPL), for dystonia. We obtained simultaneous multitracking microrecording. The lead was 3389 for Parkinson and 3387 for dystonia. All electrodes have been locked on the skull with the stimlock system. All dystonic patients received RC (rechargeable system) while parkinsonian patients had PC. Electrode position has been postoperatively confirmed by axial tomography, fused with preoperative MRI. There was no complications.

RESULTS AND CONCLUSIONS

Since a long time we have used a stereotactic frame in DBS surgery. From January 2010 we replaced this technique with the frameless Nexframe system. It's a technique guided directly by the image, it means that we can directly visualize the nuclei on 3T-MRI and reach them with a navigational system. Surely is more comfortable, less invasive and less time consuming, which may compensate the cost of the material.

The literature and our preliminary experience, based on postoperative radiological and clinical data, confirm the same reliability and precision of the frame. We think that the Nexframe with the image guided surgery is a good alternative of stereotactic frame in DBS surgery.

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EVALUATION OF THE ACCURACY OF THE STEREOPOD, A NEW GUIDANCE SYSTEM FOR STEREOTACTIC NEUROSURGERY

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Objective: This work describes the results of the ex-vivo accuracy evaluation of an innovative computer-assisted guidance system for stereotactic neurosurgery, called the StereoPod, developed in our group in collaboration with the company StereoTools (Lausanne, Switzerland).

Method:

The StereoPod is made of a stereotactic tripod, a marker visible in MR and CT images, surgical planning software and an external calibration device for the tripod. The tripod is basically an adjustable guide for the insertion of neurosurgical tools such as needles, electrodes, etc. Combined with pre-operative imaging and the external calibration device, it can be easily configured such that the tool will precisely reach the target point inside the brain.

As compared to the classical stereotactic procedure that involves stereotactic frames or to alternative solutions such as neurosurgical robots, our system has several critical advantages, including its small size and light weight, a simple surgical procedure, the possibility to perform simultaneous bilateral interventions, its low cost, etc.

The most critical feature of any neurosurgical stereotactic device is its accuracy. In order to quantify it, we have developed a complete verification procedure that involves a phantom imaged by high resolution CT-Scan (voxel size 0.625x0.625x0.625 mm) and an accuracy measurement bench.

Results: Results of these ex-vivo experiments revealed that the accuracy of our surgical planning system is reliably inferior to 1 millimeter. In average we obtain the following accuracy: **0.59+/-0.46mm**.

Conclusions: Our results show a sub-millimeter accuracy that compares very favorably to that of the reference systems, i.e. the classical stereotactic frames.

ORAL POSTERS

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IMAGE GUIDED STEREOTACTIC BIOPSY FOR BRAIN LESIONS: EXPERIENCE AND RESULTS IN 200 PATIENTS

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Two hundred consecutive patients (123men/77women/20-86 years) underwent a stereotactic procedure performed homogeneously by the same surgeon, using Leksell Stereotactic System®, between January 2006 and May 2010. The pre-operative medical conditions, methods of biopsy and postoperative complications were analyzed. A 3D-MRI Gadolinium-Enhanced T1-Weighted acquisition was used to target the lesions. In 15 patients a T2/FLAIR - Weighted acquisition was added for non-enhancing lesions and merged to T1 images using FRAMELINK® software (Medtronic). In 4 patients with a contraindication to MRI assessment, 3D-enhanced-CT-Scan was used. Target coordinates and trajectories were calculated using the stereotactic software. The stereotactic procedure was realised under sedation using Propofol® (target-controlled-infusion-system) and local anaesthesia (LA) Xylocaine® 2% or LA alone (8 patients). At least 3 samples were performed for neuropathology and molecular biology analyses (and/or bacteriology). A four hours postoperative CT-Scan was performed systematically. The patients were discharged at 48 hours postoperatively when no complications. Biopsies allowed a positive histological diagnosis in 197 cases (98.5%). In 3 cases (2 cystic lesions), the biopsy was negative (necrosis, reactional gliosis or normal brain tissue). Intratumoral bleeding with a non-regressive loss of neurological function occurred in two patients (1%), both, malignant glioma and biopsied under local anaesthesia only. No trajectories bleeding was observed. One patient had a postoperative scar infection needing an antibiotherapy without long-term complications. No postoperative seizures or anaesthetic complications were observed. Morbidity 1.5%. No patient died. Stereotactic brain biopsy performed as described is a safe, reliable and reproducible way to obtain a histological diagnosis, allowing the beginning of the complementary treatment, with a rate of complications equivalent to or less than that reported in the literature. Based on this clinical experience, our data suggests that more attention should be paid to hypervascular malignant lesions with a significantly larger haemorrhage risk and we emphasise the interest of peroperative sedation to improve the patient's comfort.

MIN-CUT-SEGMENTATION OF WHO GRADE IV GLIOMAS EVALUATED AGAINST MANUAL SEGMENTATION

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Objective: Glioblastoma multiforme (GBM) is one of the highest malignant neoplasms. The multimodal therapeutical concept involves maximum safe resection followed by radiation and chemotherapy. Despite new technical and medical accomplishments (multimodal navigation, stereotactic radiation) the survival rate still only accounts approximately 15 months. For resection and clinical follow-up exact evaluation of tumor-volume is fundamental.

Methods: Our GBM segmentation method creates 3D-graph within two steps: sending rays through the surface points of a polyhedron, with its center located inside the GBM, and sampling the graph's nodes along every ray. Then, the minimal cost closed-set on the graph is computed via a polynomial time s-t-cut, creating an optimal segmentation of the tumor boundary. For evaluation we used contrast-enhanced T1-weighted MRI-datasets.

Results: Algorithm's results were evaluated against 12 manual segmentations (done by neurosurgeons) yielding an average Dice Similarity Coefficient of more than 80% (intra physician segmentation 90%). Compared with a manual segmentation that takes on average 8 ± 5.18 minutes, the overall automatic segmentation took less than 5 seconds plus one minute to review the results.

Conclusions: In this contribution, a segmentation method for GBM boundary detection that supports the time-consuming process of volumetric assessment of the tumor was presented and evaluated. Intra physician segmentation demonstrates the reproducibility performing manual boundary extraction and hence provides a quality measure for automatic segmentations. In conclusion, exact and automatic segmentation of brain tumors obtained by our novel approach is useful for planning surgical interventions concerning tumor resection and volumetric assessment in clinical follow-up.

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3-D BRAIN ULTRASONOGRAPHY. A NOVEL TECHNIQUE OF INTRAOPERATIVE VISUALISATION

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OBJECTIVES: The neuronavigation in brain tumor surgical planning is well established technique. 3-D ultrasound offers real time intraoperative navigation, adding information about brain shift and completeness of tumor resection. We present our recent experience using a 3-D ultrasound combined Neuronavigation system in 12 cases with supratentorial tumors.

METHODS: This study is a review of 12 patients with supratentorial brain tumors. Six of them harbored meningiomas, three low grade gliomas, two glioblastomas and one case cerebral metastasis. We used the Sonowand (SONOWAND AS, Trondheim) neuronavigation system in all the cases. The preoperative navigation, based on MRI scans, defined the surgical planning - approach decision, site, shape and size of the skin incision and craniotomy, and cortical and white matter dissection as well. The intraoperative 3-D ultrasound determined the borders of the tumor during the operation. Inspection using the ultrasound probe took place several times during surgery in all cases, aiming to achieve complete tumor resection.

RESULTS: Total removal was assured in 10 patients, and partial in two. The preoperative navigation was crucial for the surgical planning and the intraoperative ultrasound for the estimation of brain shift. This was calculated more than 5mm in five cases and we corrected the surgical procedure. Additionally in two glioma cases we were able to define tumor remnants during the operation and remove them.

CONCLUSIONS: Neuronavigation combined with intraoperative 3-D ultrasound consists a powerful bimodal tool which optimizes the results of the surgical resection of brain tumors.

PERFUSION MRI AS A NEUROSURGICAL TOOL TO IMPROVE TARGETTING IN TUMORS STEREOTAXIS

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Objective: Stereotactic biopsies are subjects to sampling errors essentially due to target selection. Presence of contrast enhancement as indirect marker of malignity is not reliable. The author hypothesized that perfusion weighted imaging can improve target selection in stereotactic biopsies.

Methods: We perform a study among 21 consecutives stereotactic biopsies between june 2009 and march 2010. We adapted Mri perfusion imaging to our navigator. Perfusion-weighted imaging, in adjunction to conventional MRi data, was used to determinate the target in all cases. Conventional Mri was used to determinate the trajectory.

Results: We report a linear correlation between rCBV (ratio cerebral blood volume) and vessels density (number of vessels by mm²; R=0,64; p<0,001). Perfusion weighted imaging helped for the determination of the target in 52,4% (11) cases. In all this cases, the histopathological diagnosis was a glial tumor. For glial tumors which presented contrast enhancement, perfusion weighted imaging afford a more precise target in 9 cases, a different target in 1 case and strictly the same target in 1 case. Perfusion selected sampling afforded in all these cases cellular identity and grading. rCBV was significantly associated with grading (p<0,01), endothelial proliferation (p<0,01) and vascular density (p<0,01). For the lesions with no high rCBV (≤ 1) value, perfusion weighted Mri did not help to determinate the target but was useful for the surgical management.

Conclusions: For stereotactic biopsies, perfusion-weighted imaging based targeting is a feasible method for reducing the sampling error of the histopathological diagnosis of tumours with rCBV increased by improving the target selection.

NAVIGATED TRANSCRANIAL MAGNETIC STIMULATION FOR PREOPERATIVE MOTOR CORTEX LOCALIZATION.

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Objectives: To test the feasibility of navigated transcranial magnetic stimulation (nTMS) mapping in localization of the motor cortex in patients with brain tumor or arteriovenous malformation.

Methods: Cortical motor representation mapping was performed preoperatively with nTMS. Motor evoked potentials to nTMS were recorded from hand, leg and facial muscles. During the operation, the cortex was directly stimulated by means of monopolar electric stimulation and the electrical stimulation evoked responses were observed in the electromyographical signal of the limb muscles.

Results: Five patients underwent presurgical nTMS mapping, and the data were compared with the results of the intraoperative stimulation studies in four patients. For the comparison, volume renderings of cortex and cortical veins were computed from skull stripped MRI data fused with mapping results from nTMS. In three patients the tumor was surgically removed. In one patient a biopsy was taken from the tumor. One patient was not operated due to the location of an extensive arteriovenous malformation in the immediate vicinity of the motor cortex hand representation area, as indicated by the nTMS. nTMS and intraoperative stimulation data pinpointed the same gyrus for the motor cortex representation. No adverse effects were observed in association with nTMS.

Conclusions: nTMS seems to be a feasible noninvasive method for preoperative functional motor mapping in patients with pathology in the vicinity of the motor cortex. It may assist in preoperative surgery planning.

ULTRASONOGRAPHY- ASSISTED CORPUS CALLOSOTOMY. TECHNICAL REPORT

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Objectives: To describe the anatomy of the interhemispheric fissure (IHF) by transoperative ultrasonography (ToUS), with attention to cistern morphology, vessels anatomy and longitudinal extension of the corpus callosum (CC).

Methods: A 2D ultrasound with a 3MHz endocavity transducer (Envaisier, Philips) was used to assist a callosotomy through an interhemispheric approach in a 3-yr old boy with epilepsy. The coronal plane displayed the depth on IHF and the anatomy of both cingulate gyrus (CG). Length and width of the CC were measured in a sagittal view. Length of the CC was defined as the distance between two parallel lines located the anterior, perpendicular at the most rostral aspect of the genu; the posterior, perpendicular to the tip of the splenium. The vascular anatomy was described with color- Doppler mode in the both planes.

Results: IHF depth was 34 mm. A narrow IHF was notice, with indentation of right CG over the contralateral. The length of CC at its most medial aspect was 57 mm; its width was 4.5 mm at the rostrum, 3.0 mm at the widest segment of the body. Branching of the pericallosal and callosomarginal arteries was identified.

Conclusions: We describe, for the first time, the anatomy of the IHF and morphology of the CC with ToUS applied to corpus callosotomy. These findings corresponded with operative findings and postoperative MRi. This inexpensive device can be of great use for the intraoperative planning of IHF surgical approaches, and to define the length of the CC section.

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STEREOTACTIC BIOPSY OF THE BRAIN (ABOUT 430 CASES)

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OBJECTIVE: To evaluate the accuracy of CT- guided stereotactic biopsy in making correct pathological diagnosis and choosing corresponding management of brain tumors.

METHODS: From February 2002 to January 2010, CT – guided stereotactic biopsy was performed in 430 cases patients with intracerebral lesions which were deep-seated or located in certain main functional areas. Targetting was exclusively made by CT scan. The stereotactic frame system used is the CRW-RADIONICS.

RESULTS: The patients were 313 males and 117 females. The mean age was 48 years old. Most of lesions were located in deep cerebrum. Brain tumors were diagnosed pathologically in 383 patients (89%); malignant gliomas represented 55% ;metastasis 20%;and lymphomas 6%. Intracranial hematomas after biopsy were found in 2cases with fatal evolution in one case

CONCLUSIONS: The results suggest that CT-guided stereotactic biopsy is a reliable method for histopathological diagnosis of brain tumors and it is also of great help in selecting appropriate management.

FEASIBILITY OF THE O-ARM IN STEREOTACTIC OPERATIONS

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Object:

The accuracy and usefulness of the O-arm in different phases of the DBS operation was evaluated.

Methods:

The surgical O-arm (Medtronic Inc. Louisville, CO, USA) is a mobile 2D/3D x-ray imaging system. Scanning based on a flat panel detector and cone-beam technology producing 196 slices in 13 seconds was utilized in three patients, who were treated by bilateral STN-DBS for advanced Parkinson's disease. The target coordinates were determined using the Leksell frame, 1.5 T MR-images, and the O-arm dataset. Peroperative O-arm imaging with the stereotactic CT calculation box was utilized and compared to the coordinates, which were based on using the O-arm dataset alone. The fusion of preoperative MRI images with trajectory plans and peroperative O-arm images was accomplished at the end of the operation for calculating possible aberrations.

Results:

All patients benefitted from the DBS treatment. The O-arm could be used for the calculation of the coordinates in different phases of the operations to verify the location of the micro- and/or DBS-electrodes. The concordance of the planned and accomplished trajectories was excellent.

Conclusions:

The O-arm is a feasible and simplified CT-like scanning system, which can be utilized in DBS operations. This surgical scanning system with the 3D scanning option may be capable to shorten the operation time. It gives accurate intraoperative information for the calculation of the target coordinates, and at the end of the operation it gives immediate verification of the location of the DBS-electrodes.

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THE CADAVID STEREOTACTIC SYSTEM

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All of the Cartesian Stereotactic system existing in the market derive from the system designed by Lars Leksell in 1947; consisting of a square which serves as an axis for the X, Y, and Z coordinates and of a system of approximation composed of two post and a 180 degree arc on which is located the needle or electrode; the needle is the radius of the arc and moves on the same plane. The modifications made to the Leksell model consist in using a single post and an arc of 95 degrees, in other words using only half the frame. Some systems which utilize Polar coordinates have been adapted to the Cartesian system with a centered arc.

We present a system which is completely different from in the market as the arc has been replaced by a rectangle that rotates on two posts; besides, it utilizes an arm that slides and rotates over the rectangle, this rotating arm holds the needle. The rotating arm holds the needle in such a way that the tip is always at the center point although it rotates. Both the rectangle and the needle always rotate at the same center; this system offers the possibility of reaching the target from many more angles than all other systems.

The system was designed more than 30 years ago and has been adapted to modern stereotactic techniques, with it more than 2,500 procedures have been performed. It is a compact system whose design and functionality make it useful to the Neurosurgeon in daily practice.

A. MOVEMENT DISORDERS V: PARKINSON'S DISEASE
B. PERSISTENT VEGETATIVE STATE

ORAL PRESENTATIONS

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PREDICTING SPEECH RESPONSE FOLLOWING BILATERAL STN-DBS: RESULTS FROM 55 CONSECUTIVE PARKINSON'S DISEASE PATIENTS

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Objectives:

Deep brain stimulation in the subthalamic nucleus (STN-DBS) is an effective treatment for patients with PD but its impact on speech can be variable. The aim of this study is to examine speech response prospectively in a consecutive series of patients in order to identify clinical and surgical factors associated with speech change.

Methods:

Fifty-five consecutive patients (34 men, mean age 58 ± 6.3 , mean disease duration 12.5 ± 4.7 yrs, mean off UPDRS-III 48.1 ± 17.9 , mean on UPDRS-III 12.4 ± 7.8 , at baseline) were assessed before STN-DBS and one year after using established and validated speech and movement scales, in all conditions, on- and off- medication and on- and off- stimulation. Primary outcome was the change on speech intelligibility (% of words understood by an independent listener) off- and on- medication. Information was obtained about exact anatomical location of the active contact in the STN area and amplitude of stimulation.

Results:

One year after STN-DBS, with patients on-stimulation, speech intelligibility deteriorated on average by 14.4% ($p = .0006$) when off-medication and by 12.3% ($p = .001$) when on-medication. Medially placed electrodes in the Left STN area were linked to worse speech intelligibility. Higher pre-operative on-medication speech intelligibility, shorter disease duration and left active contact located inside the STN proper were predictors of better speech outcome at one year off-medication/on-stimulation.

Conclusions:

Speech response to bilateral STN-DBS is variable and multifactorial with both clinical and surgical factors affecting the outcome. Location of the electrode medial to the STN has a negative impact on speech intelligibility probably by affecting the fasciculus cerebellothalamicus.

RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, SAFETY-TOLERABILITY STUDY OF INTRACEREBROVENTRICULAR ADMINISTRATION OF SNN0031 (RHPDGF-BB) TO PATIENTS WITH IDIOPATHIC PARKINSON'S DISEASE (PD), USING AN IMPLANTED PUMP SYSTEM: ON-GOING CLINICAL TRIAL

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Introduction: By the time symptoms appear, patients with Parkinson's disease (PD) have lost the majority of the dopaminergic neurons. Administration of growth factors with a trophic effect on neural stem cells, such as platelet derived growth factor BB (PDGF-BB) is one possible approach to restore dopaminergic function. In a rat model of PD, administration of sNN0031 has been shown to restore dopaminergic function via activation of cell proliferation, a mechanism also implied in non-human primate models of PD using sNN0031. The ongoing clinical trial is a first-in-man study of intracerebroventricular administration of sNN0031 to PD patients.

Study Objectives: To explore the safety-tolerability of intracerebroventricular administration of sNN0031 to PD patients with moderate disease.

- To explore clinical trends and biomarkers associated with disease progression.

Design: This is a randomized, double-blind, placebo-controlled trial in a total of 12 patients at 2 study sites in Sweden. Following implantation of a pump system, patients receive investigational treatment for 14 days followed by a 3-month observation period.

Safety assessments include: ECGs, vital signs, clinical assessments, collection of adverse events, MRI, fundoscopy, assessment of visual field, CSF analysis. Disease-related parameters include: UPDRS, concomitant treatment, MADRS, MMT, EQ-5D, ¹¹C-PE2I PET imaging.

Current Status: To date, 7 patients have received investigational treatment, 5 men and 2 women, with a mean age of 65 years. All patients have tolerated the study procedure and drug administration well. An overview of adverse events and preliminary safety data will be presented.

Conclusions: Future directions for clinical development will be discussed.

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EFFECT OF DEEP BRAIN STIMULATION ON NEUROPSYCHIATRIC FUNCTION IN A RAT MODEL OF PARKINSON'S DISEASE

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Objectives: Deep brain stimulation (DBS) of the subthalamic nucleus (STN) is used to treat motor symptoms in Parkinson's disease (PD). Recently more attention has been paid to neuropsychiatric disturbances caused by PD itself and by STN-DBS. In the 6-hydroxydopamine (6-OHDA) PD rat model we investigated the effect of STN-DBS on motivation and deficient sensorimotor gating induced by the dopamine receptor agonist apomorphine.

Methods: Male Sprague-Dawley rats with bilateral lesions of the nigrostriatal dopamine system (striatal injection of 6-OHDA or vehicle for sham-lesion) were bilaterally implanted with electrodes into the STN. After determination of the individual thresholds for side effects rats were stimulated (130Hz, 80µs pulse width) or sham-stimulated for epochs of five days. After each epoch rats were tested for motivation to lever press for pellet-reward in a Skinner box. Additionally, rats were tested for prepulse inhibition (PPI) of startle after apomorphine- and vehicle-injection, an operative measure of deficient sensorimotor gating seen in certain neuropsychiatric conditions.

Results: Rats with 6-OHDA induced lesions were less motivated to lever-press for reward than sham-lesioned rats ($p < 0.05$), which was not affected by STN-DBS. The apomorphine-induced PPI-deficit was further deteriorated by STN-stimulation in sham-lesioned ($p < 0.05$), but not lesioned rats. In lesioned rats startle reaction was enhanced by the combination of STN-DBS and apomorphine ($p < 0.05$).

Conclusions: These data suggest that STN-DBS affects the neuronal circuitries responsible for certain neuropsychiatric symptoms after dopamine receptor activation. With respect to functional neurosurgery, STN-DBS may worsen deficient sensorimotor gating and increase anxiety in PD patients.

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**Pallidal Deep Brain stimulation (DBS) in Chorea Huntington
Preliminary results of a phase I trial**

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Introduction:

At present, there is no effective treatment or cure for Huntington's disease (HD) patients. Therefore, neural stem cell transplantation seemed to offer a potential treatment for HD patients that may slowdown this devastating illness. However there remain major concerns in transplantation. Therefore our group looked for alternatives, utilizing Deep Brain stimulation (DBS), based on the long-lasting successful treatment of other neurodegenerative movement disorders like Parkinson's disease (PD). Questions remained concerning the optimal target.

Methods:

This phase I clinical trial is based on the hypothesis that deep brain stimulation of the internal pallidum can reduce choreatic symptoms in 6 HD patients. In addition, this trial should demonstrate which target point within the pallidum can be used effectively for specific features of HD in order to further refine this promising strategy for a phase II multicenter trial approach. We report on six consecutive cases who underwent DBS of the Pallidum (GPi/GPe region). Electrodes were stereotactically implanted under general anaesthesia, followed by the implantation of a neurostimulation system (Kinetra, Medtronic). Patients were randomized to be stimulated into the Gpi or GPe and cross over, each for 6 weeks. Than best contact stimulation was applied for 3 months.

Results:

No perioperative complications occurred. The coordinates for the active contacts in the GPi/GPe range were adapted to individual anatomical changes. Under DBS of the pallidum choreatic movements could be reduced by median of 70% in UHDRS (range 50 to 80). The quality of life (ADL) was significantly improved in five patients. Since the effects are delayed, the adjustment and testing of the remaining contacts took place in the course of 6 months postoperatively. The most effective active contacts were in projection of the border of GPi and GPe.

Conclusion:

Systematic positive influence of DBS in Huntington's disease patients is reported for the first time. In the context of the following study it will have to be clarified whether the internal or the external part or other targets are suitable for DBS and which long-term results can be obtained.

5/OR79

CORTICAL ACTIVATION BY THALAMIC STIMULATION (CATS) A PROSPECTIVE STUDY OF THE EFFECTS OF THALAMIC STIMULATION IN MINIMALLY CONSCIOUS AND VEGETATIVE STATE PATIENTS DESCRIPTION AND AD INTERIM RESULTS.

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The CATS study (ClinicalTrials.gov Identifier: NCT01027572) is a prospective multi-institutional study on the effects of deep brain stimulation of the anterior intralaminar thalamic nuclei and adjacent paralaminar regions of thalamic association nuclei bilaterally in vegetative patients and in patients in minimally conscious state. The study started in 2009 and 3 (2 vegetative and 1 minimally conscious) patients have already been implanted. Before and after implantation all patients that displayed an alteration of consciousness stable for at least the six months preceding surgery, were evaluated using the CRS-R and Coma/Near Coma scales, functional MRI (both evoked and ongoing activity), EEG, visual, somatosensory and auditory evoked potentials. During the operation for the implantation of the macroelectrodes we also performed multiple microelectrode single neuron recordings of both spontaneous and graded tactile stimuli evoked activities from the thalami. In this setting the effects of acute electrical stimulation through one of the implanted microelectrodes on the resting and evoked (graded tactile stimuli to the contralateral hemisoma) thalamic activity were studied. They were variable from patient to patient and not only according to the current parameters adopted. Despite a relatively short average follow up time of 6 months (min 3, max 10) in all cases we had an increase in desynchronization and an enrichment of the power spectrum EEG frequencies, with improvement of the CRS-R and Coma/Near coma scores. However, none of our patients regained spontaneous behaviour suggestive for a return to a fully conscious status.

6/OR80

CONSCIOUSNESS IN NON-RESPONSIVE PATIENTS: EEG AND fMRI DATA

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Objectives: Is there a way to assess consciousness in apparently non-responsive patients? The present study attempts to address this question by measuring electrical and hemodynamic brain activity.

Methods: EEG was recorded during verbal stimulation with (a) familiar (autobiographical) vs. unfamiliar words and (b) motor ("move your hand") vs. non-motor commands in 14 patients with persistent vegetative state (PVS) or minimally conscious state (MCS) and in 9 healthy controls. From these, 10 patients and 4 healthy controls had fMRI recordings during similar conditions.

Results: A common pattern of EEG responses appeared in healthy volunteers, mostly in inter-electrode coherence of the 10-12 Hz frequency. Similar but weaker patterns appeared in 9 out of 14 patients with PVS/MCS, in various frequencies. Moreover, fMRI responses were present in all 4 healthy volunteers, and in 8 out of 10 patients with PVS/MCS.

Conclusions: Electrophysiological and hemodynamic measures of brain activity may help assess consciousness in apparently non-responsive patients. This procedure may help selection of patients for possible neurosurgical treatment with deep brain stimulation.

ORAL POSTERS

1/OP72

Combined deep brain stimulation and frameless stereotactic radiosurgery in the treatment of bilateral Parkinsonian tremor in the elderly: target selection and case report of two patients.

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Object. Considerable positive experience in functional radiosurgery with Gamma knife and linear accelerators has been reported since first Leksell's first experience in 1951, but the development of similar procedures using frameless radiosurgery devices was limited because the absence of a rigid stereotactic head frame made it difficult to identify invisible functional treatment targets. In this paper we report on two cases of bilateral Parkinsonian tremor successfully treated with DBS on one side and CyberKnife frameless radiosurgery on the contralateral side. We focus on the methodology developed to define the three-dimensional target coordinates for frameless radiosurgery.

Methods. In December 2005 and September 2007 two patients suffering from a disabling upper-limb parkinsonian tremor underwent frameless radiosurgical VOA-VOP thalamotomy. To accurately identify the treatment target the CT gantry was treated as a stereotactic frame; a rototranslation between the origin of the screen and the origin of the stereotactic atlas allowed us to obtain atlas-registered X, Y, and Z coordinates in millimeters of each point on the CT axial brain slices

Results. Both patients achieved complete bilateral tremor control by unilateral radiosurgery and contralateral DBS.

Conclusions. We developed a method for determining the 3D coordinates of a known functional target to treat with frameless radiosurgery. Based on initial trial with two patients, CyberKnife radiosurgery appears to be an alternative treatment for Parkinsonian upper limb tremor in the presence of increased surgical risks for DBS placement.

PERFUSION BRAIN SPECT IN ASSESSING MOTOR IMPROVEMENT AFTER DEEP BRAIN STIMULATION IN PARKINSON DISEASE

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Objectives: The aim of the present study was to assess regional cerebral blood flow (rCBF) changes related to motor improvement after STN DBS.

Methods: Twenty-one PD patients (11 females and 10 males, mean age 63±8, mean disease duration 11.5±4.8, mean Hoehn and Yahr stage:2.9±0.8) underwent two rCBF SPECT studies at rest, once preoperatively in the off-meds condition and the other postoperatively (at 6±2 months) in the off-meds/on-stimulation condition. Neurogam software was used to register, quantify and compare two sequential brain SPECT studies of the same patient in order to investigate rCBF changes during STN stimulation in comparison with preoperative rCBF.

Results: All patients showed a maximum clinical improvement during the first months after surgery resulting in a 42% reduction of the UPDRS motor score. The effect of STN-DBS from the pre- to the postoperative condition at 6 months was to produce rCBF increases in the pre-supplementary motor area (pre-SMA) and the premotor cortex (PMC) (mean rCBF increase=10.2%), the dorsolateral prefrontal cortex and in associative and limbic territories of the frontal cortex (mean rCBF increase=8.2%). A correlation was detected between the improvement in motor scores and the rCBF increase in the pre-SMA and PMC ($r=.89$, $p<.001$).

Conclusions: Our study suggests that STN stimulation leads to improvement in neural activity in the frontal motor/associative areas. The correlation between motor improvement and rCBF increase in higher order motor cortical areas suggests that even the short term stimulation achieves its therapeutic benefit by restoring the activity within these cortical regions.

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SKIN COMPLICATIONS FOLLOWING DEEP BRAIN STIMULATION: A TEN YEAR REVIEW AT A SINGLE CENTER

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Objectives:

DBS is an accepted method for the treatment of movement disorders. Skin complications are a well known problem after DBS (5.7% -24%) which could limit the benefit effect for the patients. In our institution we performed deep brain stimulation since 1999. The aim is to analyze the data of over 500 operated patients focused on skin complications in a single centre.

Methods:

All 537 patients which had undergone DBS in our department from January 1999 to March 2010 were retrospectively analyzed to evaluate skin complications after surgical performance. We recorded frequency, localization, agent, time course and patient risk factors.

Results:

In total 13 patients had skin complications. The focus of the infection was the pocket of the generator in 5, along the electrodes in 4, 4 patients had superficial skin lesions. The agent found was Staph. aureus. (n=8), Staph. Epidermidis (n=2), Enterobacter cloacae (n=1).

The generator was explanted in 8 cases, in 3 cases the whole system had to be removed. The age varies from 15-73 years (mean 52.8 y). The indication for DBS-surgery was Parkinson's disease (n=5), Dystonia (n=5) and essential tremor (n=2). Risk factors occurred in terms of insulin depending diabetes (n=1), hypertension (n =4) and treatment for depression (n=2), dental abscess (n=1). Over 90% occurred in the first 5 months after the procedure.

Conclusions: In our department, skin complications are uncommon (2.2%), but could also occur after years.

We have not yet identified statistically significant risk factors. To avoid skin complications a careful patient selection and performance of surgery is obligate.

4/OP75

ELECTROPHYSIOLOGICAL MAPPING USING BACKGROUND MULTI-UNIT ACTIVITY AND LOCAL FIELD POTENTIALS FOR TARGETING SUBTHALAMIC NUCLEUS

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Aim: To investigate the use of background neuronal activity as a method to improve the accuracy of the target localization for the implantation of deep brain stimulation (DBS) electrodes.

Methods: In 15 patients who underwent bilateral implantation of DBS electrodes in the Subthalamic Nucleus (STN), anatomical direct targeting was refined based on electrophysiological functional mapping, using a FHC Guideline 4000 recording system. The functional mapping included recording neuronal activity using microelectrodes and performing electrical stimulation. On targeting 12 out of 30 STN, short 2-second segments of data were recorded periodically along the entire electrode trajectory on three simultaneous tracks (typically). Neuronal activity in the frequency band 500 to 6000Hz was recorded, then separated into single and multi-unit activity (MUA) using an unsupervised wavelet thresholding algorithm. On the initial trajectory, we also simultaneously recorded LFP's in the band 0.5 to 100Hz.

Results: The MUA power showed a significant enhancement in the target region compared to the baseline with a factor of 3.07 ± 1.47 (Mann-Whitney U-test $p < 0.0001$, $n=12$). The LFP power in various bands had more complex spatial distributions, and more variability across patients, presenting the distinctive feature of a larger power in the thalamic region. As a result of the functional mapping, 6 of the 12 trajectories (50%) required lateral corrections for an optimal placement of the DBS electrode.

Conclusions: Background neuronal activity can be used to refine the targeting of the STN in patients with Parkinson's disease.

A NEW STANDARD SPACE FOR THE GÖTTINGEN MINIPIG BRAIN

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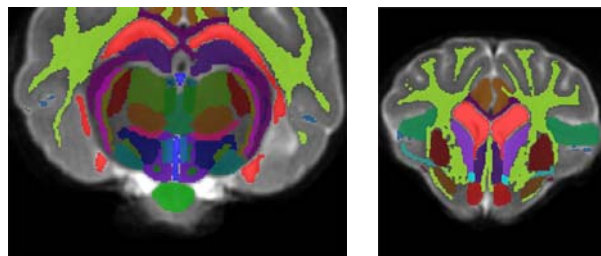
OBJECTIVES: To develop a high-resolution, MRI based atlas of the Göttingen minipig brain, to segment the atlas and estimate volume and variability for each structure.

BACKGROUND: Experimental neurosurgery in animal models of disease, particularly non-human primates, has become increasingly controversial. Göttingen minipig models have been suggested as a suitable alternative. Our group has previously generated a MRI based atlas using linear transformation techniques. Further, we have previously demonstrated that a stereotaxic space can be generated due to morphological consistency between subcortical landmarks in the minipig. The previous atlas is appropriate as PET-template, but with low contrast and blurred boundaries between structures not suitable as a tool in experimental neurosurgery in this species.

METHODS: The atlas was derived from 10 inversion recovery images obtained in vivo. An average MRI model was generated using nonlinear registration techniques in order to enhance signal and contrast-to-noise in all brain structures. Structures were manually defined based on comparative anatomy. Structural variability was assessed by using inverse nonlinear transformations to warp the labels back to each of the original MRIs. Geometric surfaces were also generated from each of the structures in order to enhance visualization for the users of the atlas.

RESULT & CONCLUSIONS: Very high definition anatomy was achieved allowing identification of structures merely visible in the individual animals. 90 cortical, subcortical and brain stem structures were labeled, mean volume calculated and variability estimated. The full result is presented in both a methodological paper and as a stereotaxic atlas.

Below, images demonstrating the subcortical labels at the level of 1: the subthalamic nucleus and mid-thalamus 2: the crus posterior of the anterior commissure.



6/OP77

PERSPECTIVE IN NANO-NEURAL ELECTRONIC IMPLANTS WITH WIRELESS POWER-FEED AND SENSORY CONTROL

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New medical device technology is essential for diagnosing, monitoring, and curing wide spectrum of diseases, anomalies and inflictions. For neural applications, currently available devices are generally limited to either a curing or a probing function. In this paper we review the technology requirements for new neural probe and cure device technology currently under development. The concept of probe-pin device that integrates the probes for neurochemistry, neuroelectricity, temperature and pressure into a single embodiment with a wireless power transmission was designed for the purpose of deep brain feedback stimulation (DBFS) with in-situ neural monitoring. The probe considered for monitoring neurochemistry is a micro-spectrometer. The feature and size of micro-spectrometer are defined for the DBFS device. Two types of wireless power transmission technology were studied for DBFS device operation. The test results of pig skin showed that both power transmission technologies demonstrated the feasibility of power feed through human tissue.

Keywords: neural probe, probe-pin device, wireless power feed, rectennas

DETECTION OF EXTRACELLULAR ALPHA SYNUCLEIN: A NEW DIMENSION IN UNDERSTANDING THE PATHOGENESIS AND TREATING PARKINSON'S DISEASE

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I. OBJECTIVES

Parkinson's disease (PD) is the second most common neurodegenerative disorder. Even though its exact pathogenesis is still unknown, the neuronal protein alpha synuclein (AS), is genetically and biochemically linked to its manifestation.

AS lacks a signal peptide sequence and until recently it was considered to exert its pathogenic effects in the cellular cytoplasm. However, recent *in vitro* studies suggest that AS can also be detected extracellularly, probably through an exosomal mechanism of secretion.

Our study aims to confirm *in vivo* the extracellular presence of AS in both humans and animal models.

II. METHODS

In our study we used *in vivo* microdialysis to investigate the extracellular presence of AS in the brain parenchyma of mice and humans. To quantify AS in our microdialysis samples, we have developed a novel sensitive sandwich ELISA coupled with a chemiluminometric assay. Mice samples were collected from the striatum of wild type and transgenic (knock out and overexpressing) animals. Human samples were collected from patients who were treated in the ICU for severe head injury and for whom microdialysis was part of their routine neuromonitoring.

III. RESULTS

Alpha synuclein was readily detected in all our samples, both human and mice, with the exception of those from knock out mice.

IV. CONCLUSIONS

Our study shows for the first time that AS is physiologically secreted in brain parenchyma. We hypothesize that the levels of secreted AS may contribute to PD initiation and/or spread through a paracrine mode of action. In this respect, extracellular AS could be a potential therapeutic target for future approaches.

IMPULSIVITY TESTING AND EEG FOLLOWING DBS IMPLANTATION IN PATIENTS WITH PARKINSON'S DISEASE

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The aim of this ongoing study is to understand how the implantation of electrodes for deep brain stimulation (DBS) affects impulse control in patients with Parkinson's disease (PD).

Materials and Methods: Patients scheduled for DBS implantation in the subthalamic nucleus (STN) are recruited initially for intra-operative impulsivity testing (auditory GoNogo) with EEG signal collection from the STN. At 3 and 6 months follow-up evaluations, patients participated in three tests providing visual stimuli (GoNogo, Simon, StopSignal), while EEG signals are collected via 32 surface electrodes. This test battery is offered twice within a 3 hrs interval, once with the stimulator working regularly and once with the stimulator switched off. So far, 15 patients have been tested in the intra-operative and five in the post-operative setting.

Results: The number of correct reactions of the 'go' type was decreased at both 3 and 6 months after DBS implantation when the stimulator was switched off. However, the effect was less pronounced at 6 months. Surprisingly, the number of correct as well as for incorrect reactions of the 'stop' type was almost unaffected by the functional state of the stimulator unit at either 3 or 6 months after DBS implantation.

Conclusions: Response accuracy improvement on go trials and no significant changes on stopping trials suggest – contrary to current models and if confirmed in a larger patient sample - an alternative functional/anatomical pathway for stopping an ongoing response not involving the STN.

This study was supported by the German Ministry of Education and Research (BMBF).

9/OP80

COMBINED-CONTROLLED INTRATHECAL INFUSIÓN THERAPY IN FIXED FLOW RATE PUMPS. UTILITY OF A SOFTWARE SUPPORT

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Argentina

Despite of the lack of FDA andapproval, combination of intrathecal drug is a popular strategy to deal with chronic pain, oncologic pain and spasticity as well.

Several guidelines from expert's consensus meeting advocates its advantages.

Among them can be described needs of minor daily dose of each drug, enhancements of their respective performance with less side effects, reduction of the cumulative amounts of active metabolites,etc..

Defining the exact amount of daily dose of each drug is a mathematical task that can be effectively accomplished by using specifically designed software.

We will present the utility of incorporating such software in the daily management of patients with chronic and oncologic pain and spasticity as well.

A. MOVEMENT DISORDERS VI: DYSTONIA
B. CEREBRAL AND CARDIAC PROTECTION

ORAL PRESENTATIONS

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CERVICAL DYSTONIA SYNDROM RELIEF UNDER PALLIDAL DEEP BRAIN STIMULATION IN GENERALIZED, SEGMENTAL, AND FOCAL DYSTONIA

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Pallidal deep brain stimulation (GPi-DBS) is a treatment of rescue in severe primary dystonia. We aimed to evaluate the GPi-DBS effect particularly on the cervical dystonia syndrome (CDS) in focal (cervical), segmental, and generalized dystonia.

Thirty seven patients with medically refractory primary dystonia were operated for continuous high-frequency GPi-DBS (11 patients with cervical and 26 patients with generalized or segmental dystonia, mean age at surgery 39.3±15.2 years, age of dystonia onset 27.6±16.8 years, disease duration 12.1±10.9 years). Eight patients had torticollis-predominant, 13 laterocollis-predominant, 9 retrocollis-predominant, 4 anterocollis-predominant CDS and in 3 patients the complex CDS pattern was observed. We assessed CDS severity in all patients according to TWSTRS and Tsui-Scale before surgery and at the end point of postoperative follow-up (34.6 months, range 6-79).

The average improvement of CDS compared to preoperative clinical state comprised 49.0±19.7% and 57.2±18.7% in TWSTRS severity subscore and TS-score, respectively. No significant difference was revealed in CDS relief between focal, segmental, and generalized dystonia. The degree of clinical improvement correlated negatively with duration of CDS (TWSTRS, $r=-0.482$, $p=0.003$). Regarding the CDS subtypes (Tsui-Scale) the best results were achieved in retrocollis (69.6±20.6%, $p=0.054$), the moderate in torticollis and anterocollis (61.5±18.7% and 59.8±10.0%), and the worst in laterocollis and complex CDS patients (48.0±15.9 and 45.5±12.0, $p=0.004$).

Thus, GPi-DBS shows the reliable efficacy in all CDS subtypes with advantageous outcome in retrocollis and less relief extent in laterocollis or complex CDS patients. Moreover, disease duration seems to be crucial. Further studies in larger population are required.

DBS IN SECONDARY DYSTONIA: CLINICAL RESULTS AND FUNCTIONAL NEUROIMAGING FINDINGS IN 9 PATIENTS.

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Objectives: Deep Brain Stimulation (DBS) represents a well established treatment option for medically intractable primary dystonia. However, the procedure's role in the management of secondary dystonia is less conclusive. The purpose of the present study is to determine the clinical benefit of DBS surgery in a series of secondary dystonia, as well as to evaluate the stimulation's hemodynamic effects, using Single Photon Emission Computed Tomography (SPECT).

Methods: Nine patients with secondary dystonia, refractory to any conservative treatment, underwent DBS surgery. Burke–Fahn–Marsden Dystonia Rating Scale (BFMDRS) was used for the clinical assessment of dystonia before and after surgery. Brain SPECT was performed post-operatively in the two stimulation states (ON-DBS and OFF-DBS) and the changes of regional Cerebral Blood Flow (rCBF) in the 3 following brain regions of interest (ROIs): Primary Motor Cortex, Premotor and Supplementary Motor Cortex and Prefrontal Cortex, were evaluated.

Results: Clinical response to DBS varied among patients. A mean improvement of 51.1% (0 – 90.7%) in BFMDRS total scores was found post-operatively. Brain SPECT imaging analysis revealed an overall decrease in CBF in the investigated ROIs, during the ON-DBS state. The observed decrease of perfusion in the presence of DBS was positively correlated with the degree of post-operative clinical improvement.

Conclusions: DBS may be a reasonable choice for severely disabled patients with secondary dystonia who otherwise have limited therapeutic options. Moreover, this study indicates a putative role of brain SPECT imaging as a postoperative indicator of clinical responsiveness to DBS.

LOBUS PALLIDUS INTERNUS AS TARGET FOR CHRONIC HIGH FREQUENCY STIMULATION IN GILLES DE LA TOURETTE SYNDROME – A CRITICAL ANALYSIS

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Objective: Significant improvement has been reported for the Globus pallidus internus (GPi) as target for deep brain stimulation (DBS) in Gilles de la Tourette syndrome (GTS). However, according to our experience, there also seem to be obvious “non-responders”. Aim of the present analysis was therefore to focus specifically on the GPi and its “sub-targets” (posteroventrolateral vs. ventromedial part) in order to provide indications for the GPi as DBS-target in GTS.

Methods: A Medline search (criteria: “Deep Brain Stimulation”, “High Frequency Stimulation”, “Gilles de la Tourette Syndrome” and “Globus Pallidus internus”) was performed. Results were reviewed with emphasis on target, stimulation parameters and clinical outcome with regard to the Munich experience (4 patients included in a pilot study).

Results: The Medline search revealed 7 reports on a total of 9 patients, all of which showed a major remission after GPi-DBS (4 posteroventrolateral, 4 ventromedial, 1 not stated). No significant difference between the two “subtargets” could be detected. Additional symptoms like SIB and OCB have only been documented completely in one report. In our own patient cohort we observed a significant variety in outcome with regard to tic-improvement (2 responders (100%/75% improvement) vs. 2 non-responders). Relating to behavioural disturbances, our own results gave a subtle hint that vocal tics and SIB might be well-treated by posteroventrolateral GPi-DBS.

Conclusion: The posteroventrolateral as well as the ventromedial part of the GPi seem to offer a promising DBS-target in GTS for selected patients. Whether there is superiority of one or the other is currently subject to ongoing studies.

FIVE-YEARS FOLLOW-UP OF 11 PATIENTS TREATED WITH GPI DEEP BRAIN STIMULATION FOR SEGMENTAL OR MULTISEGMENTAL DYSTONIA.

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Aims: GPI-DBS is a proved treatment for generalized primary dystonia, but it may be effective also for other forms of primary dystonia. We analyzed motor and disability score (BFMDRS) after a 5-years mean follow-up of 11 patients treated with GPI-DBS for Primary Segmental Dystonia.

Methods: We selected 8 males and 3 females affected by Primary Segmental Dystonia, after failing of all non-surgical therapies. In each case we targeted bilaterally the GPi with intraoperative neurophysiological refinement. Repeated measures with Bonferroni correction has been applied for the statistical evaluation of clinical data obtained with Video-BFMDRS.

Results: The mean BFMDRS total motor score improvement was 49,4% ($\pm 15,1SD$) at 1-year follow-up and 63,8% ($\pm 21,1SD$) at 5-years follow up. The statistical analysis showed the best and early results in axial subitems and significant improvement in eyes, speech and swallowing subitems. The BFMDRS disability score resulted significantly improved (46,2% at 1-year and 63,3 % at 5-years). We did not report any surgical complication. The mean voltage is 2,5 V ($\pm 1,3SD$), mean pulse-width 206 μ sec ($\pm 120,9SD$), and mean frequency 130 Hz ($\pm 5SD$). We set up monopolar configuration in all the cases but in one (double-monopolar). After 5-years all the patients underwent at least to one IPG replacement for battery exhaustion. The mean duration of IPG was 41,4 months.

Conclusions: GPi DBS seems an effective, safe and completely reversible treatment also for Primary Segmental Dystonia. The stimulation's effect on motor symptoms and patients' quality of life is good in the short-term and results steady after 5-years.

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NEUROSTIMULATION WITHDRAWAL ACCOMPANIED BY PERSISTANT CLINICAL REMISSION AFTER LONG-TERM PALLIDAL DBS IN CERVICAL DYSTONIA: A CASE REPORT

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Chronic DBS of the postero-ventro-lateral globus pallidus internus (GPi) is proved to be effective in medically refractory primary generalized, segmental, and focal dystonia with the promising long-term outcome. We report a case of stimulation withdrawal during one year after the five-year GPi-DBS in patient with cervical dystonia (CD) accompanied by persistent clinical relief. Only few descriptions of similar cases in CD and segmental dystonia are available in literature.

A 49-year-old man with the four-year history of disabling intractable primary CD (predominantly phasic retrocollis, TWSTRS total score 60, severity subscore 26) underwent the bilateral implantation of GPi-electrodes in May 2004.

After six months of continuous high-frequency stimulation, the DBS effect was evaluated as unsatisfactory and the reimplantation of both electrodes was performed. Since the reoperation, the patient showed excellent results with gradual improvement of motor function comprising almost 100% at the fifth year of follow-up. We performed the first routine replacement of pulse generator (IPG, Kinetra) 24 months after implantation. The next IPG depletion was revealed in May 2009, and the patient switched off the neurostimulator by his own. No noticeable change in clinical state or dystonia recurrence was observed and IPG was removed. Currently, one-year DBS withdrawal is achieved, while TWSTRS severity and disability subscores are preserved at zero.

To conclude, GPi-DBS may lead to sustained remission of CD, which sometimes persists for a long period even after complete neurostimulation cessation. The particular mechanisms of such effect remain unknown assuming possible changes in neuronal plasticity under the continuous DBS.

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USE OF CERVICAL SPINAL CORD STIMULATION IN TREATMENT AND PREVENTION OF ARTERIAL VASOSPASM AFTER ANEURYSMAL SUBARACHNOID HEMORRHAGE

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Cervical spinal cord stimulation (cSCS) may, hypothetically, prevent or treat arterial vasospasm in patients after aneurysmal subarachnoid hemorrhage (aSAH). Here we analyze results of the pilot human study recently completed in our institution.

Materials/Methods:

We implanted percutaneous cSCS electrodes in 12 aSAH patients immediately after their ruptured aneurysm was coiled or clipped. All patients were continuously stimulated for 14 days or until discharge while monitored for clinical and angiographic vasospasm. Subsequently, they were followed for 12 months at regular intervals.

Results:

Mean age of 12 patients was 49 years (range–27–62), average H&H grade–2.9, Fisher–3.3. Three were coiled and 9 – clipped. There was 1 unrelated death and two electrode pullouts but no complications related to the electrode insertion or to SCS during the study. Angiographic vasospasm occurred in 6/12 patients, and clinical vasospasm – in 2/12; no patient suffered any vasospasm-related neurological complication. Although preliminary results (reported earlier) showed the incidences of clinical and angiographic vasospasm smaller than predicted based on Fisher/H&H grades, we found a correlation between position of active contacts within SCS electrode and vasospasm occurrence. It appears that clinical vasospasm occurred only in those patients who were stimulated at mid-cervical level (C4-5) and not in those where active contacts were above C4.

Conclusion:

Location of active cSCS contacts may contribute to prophylactic cSCS effects in post-aSAH vasospasm patients. Use of cSCS in aSAH patients is feasible and safe; it appears to lower incidence of cerebral vasospasm and improves overall outcome. Our findings support earlier hypothesis of possible differential location-specific effect of cSCS on cerebral vasoregulation.

INCREASED MYOCARDIAL BLOOD FLOW AFTER SPINAL CORD STIMULATION IN PATIENTS WITH REFRACTORY ANGINA PECTORIS

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Introduction: In spite of great progresses in surgical and catheter interventional techniques there is an increasing number of patients with coronary heart disease not suitable for these conventional treatment strategies. A number of patients suffer from intractable pain in spite of appropriate medication.

A recent review of the Study Group on the treatment of refractory angina pectoris of the European Society of Cardiology (ESC) recommends spinal cord stimulation (SCS) as first-line therapy.

Method: 30 patients were randomized for SCS after a strong selection protocol, according to the ESBY-Study (Mannheimer 1998). The protocol includes the Seattle Angina Questionnaire, stress tolerance (Walktest, Ergometry), heart scintigraphy and heart catheter examinations. Follow ups were conducted after 3, as well as 12 months (symptoms, walktest, ergometry, and scintigraphy, drug medication and quality of life). The quadropolar electrode was placed at the level TH1-left paramedian and after a trial period it was connected to a programmable pulse generator. By reduction of angina symptoms and a consecutive increase of exercise capacity, the patients experience a great improvement in quality of life. In addition, recent data of our own study suggest a significant decrease in myocardial ischemia – examined by MIBI-SPECT – in 23 patients under SCS. After 1 year of SCS, a significant improvement of the myocardial blood flow was registered in 16 patients, while being equal in 10. This might be a direct effect of SCS perhaps due to sympaticolysis or due to a better collateralization because of the improved exercise capacity.

Conclusion: In agreement with the study group of the ESC, we would recommend SCS as first-line therapy for refractory angina pectoris. As a matter of course, conventional treatment strategies should not be replaced by SCS.

Hence, a strict evaluation before implanting a SCS device is indispensable.

Results: The present study in 30 patients shows that SCS is an efficient therapy.

ORAL POSTERS

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DBS IN MOVEMENT DISORDERS WITH THE USE OF EITHER CONSTANT VOLTAGE OR CONSTANT CURRENT STIMULATORS

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Objectives: Deep Brain Stimulation (DBS) has been established as an effective method for treating Parkinson's disease (PD). DBS, mainly of the subthalamic nucleus (STN), treats hyperkinetic and hypokinetic symptoms of PD and ameliorates long term complications of management with levodopa. We present our experience during the period 2004 - 2009 for treating Parkinson's disease with DBS using a constant voltage stimulator.

Methods: A retrospective study of patients with Parkinson's disease who were treated with DBS between 2004 and 2009.

Results: 109 patients were operated on (39 women, 70 men), with an age ranging from 28 to 85 (mean age 64.4). Bilateral stimulation of the STN was performed in 106 patients, single sided stimulation in 1 patient and stimulation of Globus Pallidus Intermedius (GPI) in 2 patients. Overall, we observed a improvement of 59.4% in Unified Parkinson's Disease Rating Scale (UPDRS) and a reduction in the levodopa equivalence dose by 63%. Surgical complications were observed in 9 patients (4.4%) and complications regarding materials in 5 (4.5%).

Conclusions: DBS is an established, effective and safe method for the treatment of Parkinson's disease. The STN is the target of choice. A good cooperation between neurologists, neurosurgeons, psychiatrists and neuropsychologists is essential for proper patient selection and treatment. Our therapeutic results are comparable with the international standard.

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TREATMENT OF CEREBRAL ORIGIN SPASTICITY WITH CONTINUOUS INTRATHECAL BACLOFEN: FOLLOW – UP REVIEW OF 14 PATIENTS.

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INTRODUCTION: The goal of present study is to assess the benefits of managing severe spasticity of cerebral origin by using continuous infusion of intrathecal baclofen delivered via a programmable pump.

METHODS: Fourteen patients with severe spasticity of cerebral origin, who had failed to respond adequately to conservative treatment, have been treated with continuous infusion of intrathecal baclofen delivered via a programmable implanted pump. All patients underwent trial bolus intrathecal injections of 50 to 100 µg of baclofen and a reduction of at least two points on the modified Ashworth Scale had been the main criteria for the pump implantation.

RESULTS: Follow – up review of these patients has lasted between eight months and four years. All patients had a significant reduction in muscle tone and have benefited by an increased function or reduced nursing care needs. Effective baclofen doses have ranged from 110 to 850 µg/day. Three patients have suffered complications that were treated successfully.

CONCLUSIONS: Continuous intrathecal baclofen delivery via an implantable pump is a safe and effective treatment for severe spasticity of cerebral origin in cases in which other conservative therapies have failed.

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IMPLANTATION OF SMALL FIXED RATE INTRATHECAL INFUSION PUMPS IN CHILDREN

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Objective: To determine the optimal placement of implantable pumps for spasticity and dystonia in pediatric population.

Materials and Methods: Three patients were operated in 2010 with Tricumed pumps; 1) male 9 years old, weight 16 kg, 2) male 12 years old, weight 19 kg, 3) female, 14 years old, weight 33 kg.

Surgical technique: in pediatric implantation, the following factors must be taken into account:

- Panniculus adiposus (nutritional condition)
- Difficulties with the technique due to scoliosis and/or hip dysplasia
- Previous surgeries related to the abdominal wall
- Ventriculoperitoneal shunt
- Ureterostomy
- Vesicotomy
- Gastrostomy
- Colostomy

If the patient was appendectomized, the pump can be implanted on the right side, otherwise the patient could be only appendectomized by laparoscopy without implanting the pump.

Gastrostomy is indicated in cases of severe malnutrition, swallowing disorders and insufficient oral feeding.

Independent from the technique to be applied (endoscopy-radiology-laparoscopy-traditional), the gastrostomy probe and/or gastric button usually exteriorizes at the level of the left hypochondrium in the middle of the left side of the umbilical line.

Results: the 3 patients operated with this technique have evolved favorably up to date.

Conclusions: early implantation of a baclofen pump facilitates and simplifies neuro-orthopedic treatments and gastrostomy implants. With an adequate subfascial technique and smaller infusion pumps satisfactory results can be achieved.

DEEP BRAIN STIMULATION FOR IDIOPATHIC PRIMARY CAMPTOCORMIA

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Objective: Camptocormia is a seldom described syndrome, which is defined as an abnormal flexion of the thoracolumbal spine, appearing in stand up position and increasing during walking. It occurs in Parkinson`s disease or Dystonia or can appear as primary idiopathic disease. In the literature data of deep brain stimulation (DBS) for idiopathic primary camptocormia are extremely rare.

Methods: We report on two patients with primary idiopathic camptocormia. The first patient was a 54-year-old woman, who suffered from camptocormia since 18 month. The second patient was a 49-year-old man with a 1-year-history of the disease. Both reported on an acute beginning, no reason could be found and the symptomatic was drug-resistant. As a therapeutic trial we performed a bilateral stimulation of the GPI, using stereotactic MRI-planning, multiple trajectories for micro recording and macro stimulation. Surgery was performed under general anaesthesia.

Results: Along the trajectory a typical pattern of the GPI, like in other dystonic patients was found. In addition, normal thresholds for motorical side effects for an electrode position in the GPI could be detected. After starting permanent stimulation, improvement with up to complete reduction of the dystonic movement could be achieved after 2 weeks for the first patient as well as 3 days for the second patient, lasting on the follow-up period of one year respectively, 6 month.

Conclusion: Our two cases support that the deep brain stimulation of the GPI could be an effective method in the treatment of primary camptocormia. More cases have to follow in order to support the findings.

5/OP85

CASE REPORT: TREATMENT OF SECONDARY DYSTONIA IN THE SYNDROME OF LEUKOENCEPHALOPATHY, BRAIN CALCIFICATIONS AND CYSTS (LCC) BY DEEP BRAIN STIMULATION (GPi)

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Introduction: LCC is a rare hereditary disease. Caused by calcifications and cysts in the white matter as well as in the basal ganglia, the children present with developmental retardation, ataxia, dystonia and spasticity. Focal signs may vary, dependent on the location of space occupying cysts.

Case history: A right-handed 7-year-old girl developed tetraspasticity and dystoneal involuntary movements accented on the right side. Moreover, she was mentally retarded. In neuroimaging, widespread calcifications of the basal ganglia and smaller cysts of the white matter of the right hemisphere were found. Fundoscopy revealed no signs of retinal abnormality. Histologically, microangiopathy with dystrophic changes, astrogliosis, and calcifications is described. The patient – now 14-years-old – is dependend on a wheel chair. The patient´s younger sister with the same disease and a clinically worse condition is suffering from large cysts, which required neurosurgical interventions. Other family members are not affected.

To palliatively treat the dystonia, GPi DBS was considered. Because of the calcifications of the basal ganglia, it was not evident if a trajectory could be found without hitting the macro calcifications. Therefore, a 3-D-computed tomography (CT) was performed. It confirmed that the empiric target of the globus pallidus internus (GPi) itself was located outside the calcifications and that there might be passable trajectories via parietal burr holes.

After receiving informed consent of the parents, bilateral quadripolar GPi-electrodes were implanted under general anaesthesia. With stimulation the involuntarily movements of the right side are arrested. Assisted walking is feasible.

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DOUBLECORTIN-POSITIVE CELLS IN THE ADULT PRIMATE CEREBRAL CORTEX AND POSSIBLE ROLE IN BRAIN PLASTICITY AND DEVELOPMENT

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Objective:

We have recently demonstrated that adult cortical cell autografts may represent an attractive restoration alternative to bypass some limitations of fetal grafting in monkey models of Parkinson's disease and stroke.

The aim of the study is to better understand the origin of adult primate brain cells obtained in culture from the primate cortical biopsies.

Methods and results:

The cells obtained from primate biopsies first expressed DCX in culture and after a while the expression of nestin appeared. By preparing slices of cortical tissues for setting cell culture, only cell populations that expressed DCX survived *in vitro* over time. BrdU incorporation also indicated that the dividing cells were DCX-positive. Adult primate cortical tissue sections showed that DCX was expressed in a subpopulation of cells in layers 1 and 4-5 of the gray matter, in the glia limitans and in the border of the white matter. Co-immunolabelling with GFAP (astrocyte marker), NeuN and MAP2 (neuronal markers) demonstrated that there were different subpopulations of DCX-positive cells depending on their localization in the cortex.

Discussion and conclusion:

Nestin-positive primate cells can be obtained *in vitro* from cortical biopsies, as previously shown in primates. These cells can be reimplanted, they survive and migrate in a lesioned motor cortex or a dopamine-depleted striatum. These *in vitro* adult cortical brain cells originate from DCX-positive cells of the adult primate cortex. Their physiological roles in the activity and plasticity of primate adult brain and their exact function still have to be investigated. These results open new perspectives in the fields of primate brain physiology and brain repair.