Stereotactic and Functional Neurosurgery

XXIInd Congress of the **European Society for Stereotactic and Functional Neurosurgery**

Madrid, Spain,
September 28–October 1, 2016

Abstracts

Guest Editor
J. Barcia, Madrid

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Disclosure Statement

The editor has nothing to disclose.

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Brain Machine Interface and Imaging

#8426

Adaptive Deep Brain Stimulation in Parkinson's Disease, First Results

Etienne Pralong[1], Robert Leeb[2], Aleksander Sobolewski[2], Iturrate Inaki[2], Chavarriaga Ricardo[2], Peciu-Florianu Iulia[1], Vingerhoets Francois[3], Bloch Jocelyne[1], Millan Jose[2]

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Keywords: Parkinson, Brain computer interface, Neurophysiology.

Introduction: Classical DBS treatment of Parkinson disease (PD) involves constant stimulation by electrodes localized in deep brain structures such as the sub thalamic nucleus or the internalpalladium. This constant stimulation may be suboptimal facing the fact that movement planning and execution involves sequential parietofrontal network activation that is expressed by modulation of EEG beta-band oscillation often referred as event-related desynchronization and synchronization (ERD/ERS). Indeed constant stimulation of the STN is not without secondary sometimes dramatic secondary effects. In this context adaptive DBS, where stimulation is triggered by certain neurophysiological markers, has emerged as an improvement over conventional systems. It may reduce the amount of energy received by the patient and also theoretically the side effects.

Methods and Results: We recorded brain activity from the subthalamic nucleus via the deep electrodes while stimulating simultaneously. This was made possible because of the design of a custom-made system that allowed filtering out stimulation artefacts from the underlying brain signals. Tests of the closed-loop adaptive DBS have been performed in 3 PD patients. The protocol consisted of three stimulation conditions over 3 days: continuous (normal), adaptive, and no stimulation, whereby each condition was 20 min long. A blinded neurologist evaluated the clinical assessments of the motor effect via the Unified Parkinson's disease rating scale (UPDRS) before, during, and after each condition. In the no-stimulation condition, we found a pathological synchronization of the beta band in both hemispheres and a strong coherence between both hemispheres in the high-beta and low-gamma band. Therefore, detection of increased (over the 50 percentile) beta band activity (22–28 Hz) was used to trigger the stimulation in the adaptive condition. When compared, subject-specific closed loop stimulation yielded similar efficiency to conventional continuous DBS.

Discussion: Our initial results demonstrate that we can successfully record local field potentials, detect the physiological biomarkers of motor symptoms in PD patients and adaptively trigger the DBS with the same efficacy as constant stimulation. Nevertheless, more subjects and tests over longer periods of time are necessary to confirm the preliminary observations on the efficacy of adaptive DBS.

Significance: Closed-loop adaptive DBS is possible which opens up strategies to better tune the stimulation leading to increased battery life and better control over symptom variations.

#8446

Targeting Accuracy of the Subthalamic Nucleus in DBS Surgery: Comparison between 3T MRI and Microelectrode Recording Results

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Keywords: DBS, Subthalamic nucleus, Targeting, Microelectrode recording.

Backgorund: Targeting accuracy in DBS surgery is defined as the level of accordance between the selected target and the anatomically real target reflected by characteristic electrophysiological results of microelectrode recording (MER). We aimed to determine the correspondence between the preoperative predicted target based on modern 3Tesla T2-weighted magnetic resonance imaging sequences and intraoperative MER results separately on the initial and consecutive second side of surgery.

Methods: We retrospectively analyzed 86 trajectories of DBS electrodes implanted into the subthalamic nucleus (STN) of patients with advanced Parkinson's disease. The entrance point of the electrode into the STN and the length of the electrode trajectory crossing the STN was determined by intraoperative MER findings and 3T high-resolution T2-weighted magnetic resonance images with 1 mm slice thickness.

Result: The average difference between MRI-based and MER-based trajectory length crossing the STN determined in each patient was 0.28 ± 1.02 mm (–0.51 to –0.05 mm 95% CI). There was a statistically significant difference between the MRI- and MER-based entry point on both the initial and second side of surgery ($p = 0.04$). 43% of the patients had a difference of more than > 1 mm of the MRI-based predicted and the MER-based determined entry point into the STN with values ranging from –3.0 to + 4.5 mm.

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Conclusions: MRI-based targeting of the STN is accurate in the majority of cases in both the first and second side of surgery. However, in 43% of implanted electrodes we found a relevant deviation of more than one millimetre supporting the concept of MER as an important tool to guide and optimise targeting and electrode placement.

#8467

Electrode Tip Localization in Rats Using Various CT Imaging Techniques and BlockFace Is Accurate, Fast and Cheap as Compared to Histology

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Introduction: As brain implants such as electrodes to record and stimulate neural tissue in laboratory animals are becoming more and more sophisticated, implant tip localization methods have not evolved over the last century. Even nowadays, histology and copying to stereotactic atlases remains not only the gold standard but also the most commonly used method for implant tip localization, despite huge advances in laboratory animal imaging technology. We aim to compare various modalities for electrode tip localization in terms of accuracy, time and costs.

Material and Methods: In 289 g male Wistar (SD 7.8 g; n = 12) and 424 g male Sprague-Dawley (SD 6.2; n = 12) rats, preoperative CT imaging was followed by stereotactic implantation of 2 electrodes (one in each hemisphere). Next, after in vivo postoperative CT imaging (CTinvivo), unilateral electrolytic marking of the electrode tip position and euthanasia was performed. Now, an ex vivo postoperative CT with the skull and electrodes in place (CTexvivo) was followed by a 14-day iodine immersion and a new CT with and without skull and electrodes in place (CTiodine+skull; CTiodine-skull, respectively) in half of the specimens. Finally, all specimens underwent BlockFace, which is a 3D reconstruction of photographic images acquired with a digital camera facing the remainder of the paraffin block on the microtome, and histology. Six different researchers with different levels of experience picked the electrode tips either directly (when the electrode was directly visible) or indirectly via different definitions (when only the electrode track was visible).

For co-registration of the images to the Johnson-Paxinos MR-atlas, we first constructed a CT atlas based on the preoperative images of the Wistar rats. The postoperative CTs with bony anatomy were co-registered to this CT-atlas and via this atlas to the MR-atlas, while the modalities without bony anatomy were co-registered directly to the MR-atlas.

Result: All CT modalities and BlockFace allowed for electrode tip localization, with modality-specific advantages and disadvantages as compared to histology. While CTinvivo, CTexvivo and CTiodine+skull permit direct electrode visualization, CTioine-skull, BlockFace and histology only show the electrode track, that can be wider and deeper than the final electrode tip position. Depending on the target, histology and CTiodine-skull can show internal brain structures surrounding the electrode tip/trace, whereas the other modalities cannot and consequently heavily rely on the co-registration quality. Clearly, all but CTinvivo only permit localization after euthanasia, hereby only allowing subject exclusion due to erroneous implantation after completion of all tests.

Electrode tips could be reliably localized both in rats identical to and different from those used to create atlases (289 g male Wistar rats and 424 g male Sprague-Dawley rats, respectively).

Average time needed for localization of 2 electrodes in 1 rat brain (anesthesia, acquisition, preparation of chemicals, euthanasia and perfusion, brain extraction, paraffin embedding, slicing, staining, imaging post processing, tip picking) ranged from 27 minutes (CTinvivo) to 94 minutes (histology).

Average costs, as charged in our institution, for localization of 2 electrodes in 1 rat brain (anesthesia, CT use, chemicals and consumables, histological processing, microtome use) ranged from 5.50 euro (CTexvivo) to 21.24 euro (histology).

Conclusion: We conclude that CT imaging techniques and BlockFace are valuable alternatives to histology for electrode tip localization, and are both faster and cheaper as compared to histology.

#8543

Short-Term Intensive Neurofeedback Training Using Realtime fMRI in Pre-Operative Parkinson's Disease Patients

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Keywords: Real-time fMRI, Neurofeedback, Parkinson's disease.

Introduction: Neurofeedback training using real-time functional magnetic resonance imaging (rtfMRI) enables learned control of brain activity of a target brain region. This emerging non-invasive intervention has been used to produce clinical improvements in disorders such as chronic pain and recently, Parkinson's disease (PD). We report a unique intensive neurofeedback training paradigm, using rtfMRI, for PD patients undergoing deep brain stimulation surgery of the subthalamic nucleus (STN-DBS), and compare the efficacy of training against a control group of non-surgical patients also undergoing rtfMRI neurofeedback training.

Aims: The study aims to establish the feasibility of using intensive rtfMRI neurofeedback in patients with PD, with the goals of demonstrating volitional control of higher order motor cortical

activation (i.e. supplementary motor area, SMA), and linked clinical improvements, together with a potential interaction with the effects of STN-DBS.

Methods: Over one week of intensive rtfMRI training in the scanner, patients were trained to use motor imagery linked to feedback provided by a visual interface in the form of a 'thermometer bar' coupled in realtime to BOLD activation in their SMA. Patients were trained specifically to increase activation of their SMA. UPDRS assessments both on and off medication, together with finger tapping paradigms, were performed before and after neurofeedback training to investigate any improvements linked to the intervention. Functional, connectivity and structural imaging correlates were also examined. Further, in surgical patients, a possible interaction of rtfMRI-led neurofeedback with DBS will also be investigated.

Results: Behavioural, brain activation patterns, connectivity and structural correlates of rtfMRI neurofeedback training were examined in relation to observed improvements in UPDRS scores both on and off medication.

Conclusions: We provide preliminary evidence that intensive rtfMRI neurofeedback training can be successfully implemented and tolerated in PD patients, with the potential for behavioural and clinical improvements.

#8553

Subthalamic Nucleus Deep Brain Stimulation in Parkinson's Disease: Local Efficacy Regions and the Influence of Cortical Connectivity

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Keywords: Connectivity, Subthalamic nucleus (STN), Hyperdirect pathway.

Optimal stimulation site for subthalamic nucleus deep brain stimulation remains ill-defined. Previous studies have disagreed on whether contacts within the nucleus, or just superior to it, in the rostral zona incerta, give best improvement in motor symptoms. Furthermore, the effect that cortical connectivity has on predicting the success of deep brain stimulation is yet to be established. Here, we aimed firstly to identify stimulation clusters in the subthalamic region that predict maximum improvement in rigidity, bradykinesia and tremor, or emergence of side-effects; and secondly, to map-out the cortical fingerprint, mediated by the hyperdirect (subthalamic-cortical) pathway which predicts maximum efficacy. Twenty patients with Parkinson's disease underwent preoperative high angular resolution diffusion imaging prior to bilateral subthalamic nucleus deep brain stimulation. One-year after MRI-guided and MRI-verified surgery all contacts were screened for efficacy and side-effects at different amplitudes. Voxel-based statistical analysis was used on models of corresponding volumes of tissue activated to identify significant treatment clusters. Probabilistic tractography was employed to identify patterns of cortical connectivity associated with treatment efficacy. All patients responded to treatment (off medication UPDRS-III mean improvement was 46% [$p < 0.0001$] at one year) without adverse events. Clusters corresponding to maximum improvement in tremor were inside the nucleus in the posterior, superolateral portion. Clusters corresponding to improvement in bradykinesia and rigidity were closer to the superior border in a slightly more medial and posterior location. The rigidity cluster extended beyond the superior border to the area of the zona incerta and H_2 Forel's field. Cortical connectivity to the primary motor area was predictive of higher improvement in tremor; whilst that to the supplementary motor area was predictive of improvement in bradykinesia and rigidity; and connectivity to the prefrontal cortex was predictive of improvement in rigidity. Our findings support the presence of separate stimulation sites within the subthalamic nucleus and its superior border, with different patterns of cortical connectivity, associated with maximum improvement in tremor, rigidity and bradykinesia.

#8591

How Does Surface Registration Influence Position and Orientation Errors in Neuronavigation Procedures?

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Keywords: Neuronavigation, Registration, Error, Accuracy, Precision, Position, Orientation.

Introduction: Neuronavigation procedures demand high precision and accuracy. Despite this need there is still few literature analysing error in these procedures. There are many steps which could introduce significant position and orientation errors. One of these steps, is surface registration, when the image space is matched with the patient space.

Objective: The objective of this study is to evaluate the influence of the point registration method in global procedure errors using a previously designed cranial phantom.

Methods: The designed phantom consisted of a 3D plastic cranium with 10 spheres with different trajectories to their centres and 4 smaller spheres without trajectories. A cloud of points of the phantom was acquired, using the Polaris optical tracking system. Then, the centres and trajectories of the spheres were mathematically calculated and used as ground truth. Afterwards, Com-

puted Tomography and Magnetic Resonance images of the phantom were acquired to be compared with the ground truth. A neuronavigation procedure (a biopsy using the Medtronic Vertek arm and biopsy needle) was planned using Medtronic Cranial 5.2.5 and framelink 5.4.1 software and subsequently simulated. In such procedure, a standard registration, in accordance to manufacturer specifications, as well as an improved registration, which included all sides of the phantom, were executed. The biopsy needle final position and trajectory were obtained for each of the spheres using the reference system and compared with the ground truth.

Results: After execution of the procedure with a standard registration a mean position error of 5.41 mm (with standard deviation of 1.75 mm) and a mean orientation error of 3.99 degrees (with standard deviation of 1.72 degrees) was identified. After the procedure with the improved registration the mean position error decreased to 3.93 mm (with standard deviation of 1.70 mm) and the mean orientation error to 3.65 degrees (with standard deviation of 1.29 degrees).

Conclusion: Registration had an important influence on global position and orientation errors. A method which includes all the sides of the cranium was used and presented positive results in decreasing the magnitude of global errors, therefore suggesting the need for more accurate registration techniques.

Epilepsy

#7907

SEEG-Guided Radiofrequency Thermocoagulation (SEEG RF-TC): From in vitro and in vivo Data to Technical Guidlines

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Keywords: SEEG RF-TC epilepsy.

Deep brain electrodes have been used for the last ten years to produce bipolar radiofrequency thermo-coagulation (RF-TC), especially in SEEG-guided radiofrequency thermocoagulation (SEEG RF-TC). However, this technique is based on empiric knowledge and there are no available studies related to its physical effect and to the optimal settings of the RF-generator for this procedure. The aim of this study is threefold: 1) provide in vivo animal data concerning the effect of bipolar RF-TC on brain and its safety 2) assess the parameters of this procedure (dipole selection and current delivery) which produce the most efficient lesion and 3) provide technical guidelines.

First we achieved in-vivo RF-TC on rabbit brain with several conditions (power delivered from 5 to 10 W, lesioning time from 30 to 90 s) and analyzed their influence on the lesion produced. Only a difference in term of volume was found and type of histologic lesions was similar whatever the settings of RF-TC were. Moreover we did not notice any damage on SEEG electrode due to its use to perform RF-TC.

We then performed multiple RF-TC in-vitro on egg albumen (a linear correlation was found with the diameter of in-vivo RF-TC) first with several parameters of radiofrequency (power delivered from 0.94 to 7.5 W and delivered without limit) then with different dipole selections (contiguous and noncontiguous electrode contacts). The endpoint was the size of the RF thermo-lesion produced.

Using unfixed parameters of RF current delivery and increasing it until the power delivered by the generator collapsed produced significantly larger lesions ($p = 0.008$) than other conditions. Concerning the dipole selection, the use of contiguous contacts on electrodes lead to lesions with a higher volume ($p = 7.7 \times 10^{-13}$) than those produced with noncontiguous electrode contacts.

Beside the target selection in thermo-SEEG, which are summarized based on a literature review, we report the optimal parameters for RF-TC: RF-current must be increased until the power delivered collapses and dipole should always be constituted by contiguous electrode contacts.

#8434

Deep Brain Stimulation in Subiculum for Mesial Temporal Lobe Epilepsy

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Keywords: DBS, Subiculum, Mesial temporal lobe seizures.

Objective: While DBS of non-sclerotic hippocampus is highly effective in controlling seizures originated in mesial temporal lobe, DBS in hippocampus with sclerosis (HCS) has a sub-optimal and delayed effect on seizure control. This might result from decrease in cellularity and changes in impedance and network in sclerotic tissue. Recent studies have proposed that the subiculum (SC) plays an important role in the genesis and propagation of epileptic seizures, and another group report correlated improvement of seizures by DBS to the proximity of active contacts to the SC. Since in most cases of HCS the SC is well preserved, the aim of this study was to test SC-DBS in cases of mesial temporal lobe epilepsy with HCS.

Material and Methods: Seven patients with mesial temporal lobe seizures and HCS were implanted in the interface between hippocampus and parahippocampus for DBS. All had previously intracranial recordings to identify the side and precise location of seizure onset. Patients entered a randomized, double blind (DB) protocol in which, after a 4 months baseline (BL) period and one month post-implantation period OFF stimulation, 3 cases had the DBS turned ON, while 4 patients continued OFF DBS for a period of 3 months. Thereafter DBS was turned ON in all and followed

for a period of 7 months. DBS parameters were cycling mode 1 min ON/4 min OFF, 3.0 V, 450 microsec and 130 HZ. AED's were maintained unchanged along the study. The outcome for this series was compared with a similar number of cases with HCS treated by DBS in the sclerotic tissue and reported before.

Results: In BL mean total number of seizure per month for the group was 8.29 with 7.26 ending in Generalized Tonic-Clonic (GTC) seizures. Seizure number decrease during the 1st month after implantation and returned to BL levels by the 2nd month. Thereafter, there was not a significant difference between patients ON/OFF stimulation during DB period. When all patients were turned ON, there was a reduction of 56.94% in total number of seizures ($p = 0.027$) and 78.25% for GTC ($p < 0.017$), which was no different to what has been reported for DBS in HCS.

Conclusion: Electrode placement in the SC induced a transient decrease in seizures. Thereafter decrease in number of seizures was more prominent for GTC than for partial complex seizures. Therefore subiculum seems related to seizure propagation more than seizure onset.

#8485

The Surgical Approach to the Anterior Nucleus of Thalamus in Patients with Refractory Epilepsy: Experience from the European Multicenter Registry (MORE)

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Keywords: Epilepsy, Deep brain stimulation, Targeting.

Background: Deep brain stimulation (DBS) of the anterior nucleus of thalamus (ANT) is an adjunctive treatment option for refractory epilepsy patients with partial onset seizures with and without secondary generalization and is supported by the Stimulation of the Anterior Nucleus of Thalamus for Epilepsy (SANTE) randomized controlled trial. The SANTE trial utilized a transventricular (TV) approach to ANT. Traversing the lateral ventricle has been considered by some European physicians as connected to lead misplacement and/or asymptomatic intracranial hemorrhage, motivating the search for alternative techniques.

Objective: The MedtrOnic Registry for Epilepsy (MORE) is an open label observational study evaluating the long-term effectiveness, safety and performance of ANT-DBS for the treatment of refractory epilepsy. The difference in success rate of placing contacts at ANT was compared across surgical techniques from 73 ANT-DBS implants in 17 European centers participating in the MORE registry.

Materials and Methods: The success rate of placing contacts at ANT with DBS lead model 3387/3389 was evaluated using a screening method combining both individual patient imaging information and stereotactic atlas information to identify contacts at ANT.

Results: Extraventricular (EV) lead trajectory was used in 53% of the trajectories. Approximately 90% of the TV lead trajectories had at least one contact at ANT while only 71% of the EV lead trajectories had at least one contact at ANT. The success rate for placing at least one contact at ANT bilaterally was 84% for TV implants and 58% for EV implants ($p < 0.05$; Fisher's exact). No intracranial bleedings were observed but one cortical infarct was reported following EV lead trajectory.

Discussion: TV was superior to EV trajectory enabling more consistent placement of contacts at ANT and did not appear to be associated with any increase risk of adverse events which was the original concern.

Conclusion: A transventricular trajectory is recommended for ANT-DBS for its greater probability in placing contacts at ANT. The results of this registry support the use of TV approach for DBS. Further data is needed in order to confirm that TV is associated with superior patient outcomes.

#8491

Optimization of the Stimulation Site Improves Outcome after Deep Brain Stimulation of the Anterior Nucleus of Thalamus in Refractory Epilepsy

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Keywords: Epilepsy, Deep brain stimulation, Targeting, Seizure.

Background: Deep brain stimulation (DBS) of the anterior nucleus of the thalamus (ANT) is an approved form of therapy in localization related refractory epilepsy by European authorities and is currently being evaluated for approval by food and drug administration (FDA). Double blind randomized controlled trial (SANTE) showed significant 56% seizure reduction at two years (Fisher et al., 2010). Further improved results with 69% seizure reduction were observed at five years (Salanova et al., 2015). We

have recently reported that stimulation site specifically at ANT improves responder rate after ANT-DBS (Lehtimäki et al., 2016).

Objective: Here we studied the effect of stimulation site on outcome in more detail focusing on quantitative change in seizures and seizure types with respect to active contact location after ANT-DBS.

Patients and Methods: Prospective seizure counts from 16 patients with ANT-DBS for refractory epilepsy at Tampere University Hospital were analyzed. A total of 64 DBS lead contacts were stimulated in this patient group to achieve optimal outcome comprising a total of 32 patient years of active stimulation. The location of each contact was evaluated in preoperative 3T MRI STIR images (Möttönen et al., 2015) co-registered with postoperative contrast enhanced CT.

Results: In nine patients, initial selected stimulation site was bilaterally at ANT. Seven patients received initially stimulation uni- or bilaterally outside ANT followed by optimization of stimulation site into ANT in five patients by reprogramming and/or surgical replacement (mean delay 31 months). Interestingly, stimulation site bilaterally at ANT was associated with a median of 67% seizure reduction at 24 months compared to baseline ($p < 0.05$, Wilcoxon signed ranks test) while a median of 21% seizure reduction was observed after non-bilateral stimulation of ANT ($p = 0.17$). A strong trend towards significant difference between groups at 24 months was observed ($p = 0.052$; Mann-Whitney test). No significant difference was evident at baseline between patient groups ($p = 0.22$). However, optimization of the stimulation site into bilateral ANT stimulation in five patients out of seven resulted in improved 60% seizure reduction in this group by last six months carried forward analysis compared to the baseline ($p < 0.05$; Wilcoxon signed ranks test). Patients with an initial stimulation site bilaterally at ANT showed a median of 92% seizure reduction by last 6 months. The most prominent seizure reduction was observed in seizures with an interruption in awareness (complex partial seizures), while the effect in seizures with preserved awareness (simple partial seizures) or secondarily generalized seizures was modest.

Conclusions: Stimulation site at ANT is crucial for therapy response, and favorable outcome may be achieved also relatively late by optimization of the stimulation site by reprogramming or replacement of the leads. Outcome improves clearly over time after chronic bilateral stimulation of ANT being most prominent in seizures with interruption in awareness.

#8520

Deep Brain Stimulation for Refractory Epilepsy: Do Firing Patterns in the Anterior Nucleus of Thalamus Relate to Therapy Response?

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Keywords: Deep brain stimulation, Epilepsy, Anterior nucleus of thalamus.

Introduction: Therapy response to deep brain stimulation (DBS) of the anterior nucleus of thalamus (ANT) for medically refractory epilepsy varies highly among patients. Precise positioning of the DBS lead is potentially crucial to maximize therapeutic efficacy and minimize side effects. For a correct implantation, the ANT is anatomically located using pre-operative 3T MRI and perioperative microelectrode recordings (MERs). Recordings of neuronal firing patterns produce a 'popcorn popping' sound, which empirically differs among patients.

Objective: We investigate whether firing patterns in the ANT relate to therapy response in DBS for epilepsy.

Patients and Procedures: We prospectively included 10 consecutive medically refractory epilepsy patients planned for DBS surgery. Using pre-operative 3T MRI, we planned an extraventricular approach to the ANT and performed MERs along this trajectory. We compared characteristics of neuronal signals at different depths along the electrode trajectory between DBS responders and non-responders. Responders were defined as patients with a seizure frequency reduction of more than 50% at 1 year follow-up. The anatomical locations of recordings were verified using fused preoperative 3T MR-images and postoperative CT-images.

Results: We found high-amplitude neuronal bursts around the target region and in the ANT. Preliminary results suggest that responders to DBS ($n = 5$) have higher mean firing rates and higher mean firing rates within bursts near the target region compared to non-responders ($n = 5$), with a clearer delineation of firing rate at target compared to surroundings. Electrode trajectories did not differ between responders and non-responders.

Conclusion: Preliminary results suggest that firing patterns in the ANT relate to therapy response in DBS for patients with medically refractory epilepsy. Perioperative analysis of firing patterns using MERs may guide targeting and contribute to the prediction of therapy response in DBS for epilepsy.

#8845

DBS of ANT for Epilepsy – The Lisbon Experience

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Keywords: Epilepsy, Deep brain stimulation, Anterior nucleus of thalamus, DBS, ANT.

Introduction: Deep Brain Stimulation (DBS) of the Anterior Nuclei of Thalami (ANT) has a growing interest as a palliative surgery for refractory epilepsy. The bilateral ANT-DBS may have a place in focal epilepsies when no focal resection is indicated or when patients refuse resective surgery.

Material and Methods: The Epilepsy Surgery Group of the Hospital de Santa Maria (CHLN) started this approach in January 2011, and we have operated 12 patients (7 females) so far. Median time of epilepsy before implantation was 26 years (7–46) and median number of seizures per month 15 seizures/month (3–39). All patients have already tried 3 or more antiepileptic drugs. Three patients had previous epilepsy surgeries, one a VNS and other two resective surgeries.

Electrodes were implanted with Leksell® stereotactic frame with targets and trajectories obtained from FrameLink® Medtronic's software. Both 3387 and 3389 electrodes were used through a trans-ventricular cannulated approach in the majority of the patients (9/12). Post-operative control of electrode contacts was done with CT fused with pre-operative MRI and compared to published stereotactic atlases.

Results: All 12 patients have at least one contact in one ANT and 11 in both anterior nuclei. Two patients required additional surgeries due to slippage of electrode(s) to the III ventricle during a trans-ventricular approach. No intraventricular bleeding was seen in post-operative CT of all patients and no major complications related to surgery were recorded. Seizure frequency reduction was seen in more than half of the patients but almost all reported a decrease in severity of their seizures.

Approximately one third of the patients developed a newly or aggravated depression early after stimulation initiation that required medication. No suicidal ideation was found in any of them.

Discussion and Conclusions: The ideal candidates for ANT-DBS is yet to be found but the low incidence of major complications from this surgery and the reversibility of those related to stimulation makes this neuromodulation technique an option to treat otherwise difficult refractory epilepsy cases.

Multicenter studies allow us to collect more cases faster but single center series with their more standardized approach may also add some important information.

Experimental

#8303

Noninvasive Neuromodulation and Brain Mapping with Low Intensity Focused Ultrasound

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Keywords: Low intensity focused ultrasound, Neuromodulation, Brain mapping.

Objective: Recently, high intensity ultrasound has been precisely focused through the intact human skull to perform thalamotomy. Acoustic energy of lower intensities is capable of both exciting and inhibiting neural tissues without heat or tissue damage. Thus, we investigated in a large brain animal model the potential for low intensity focused ultrasound for noninvasive brain mapping.

Methods: The swine sensory thalamus was stereotactically targeted with low intensity focused ultrasound, and somatosensory evoked potentials were recorded from an epidural grid electrode. SSEP recordings were simultaneously obtained from trigeminal, median, and tibial stimulations during thalamic sonications. Magnetic resonance thermography was used tomonitor temperatureat the acoustic focus and histology was used to assess for potential tissue injury.

Results: Low intensity focused ultrasound inhibited sensory evoked potentials with a spatial resolution ~2 mm. This method could be used to selectively inhibitthalamic nuclei. Specific trigeminal SSEP suppression occurred and was transient without affecting medial or tibial SSEP. The converse was true when target-

ing the ventrolateral thalamic nucleus. There was no observed tissue heating during sonications and no histological evidence of tissue damage.

Conclusions: Low intensity focused ultrasound can be safely used to reversibly modulate deep neuronal circuits in the central nervous system. Noninvasive brain mapping with focused ultrasound is likely feasible in humans.

#8508

Motor Cortex Stimulation Does Not Lead to Functional Recovery after Experimental Cortical Injury in Rats

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Keywords: Motor cortex stimulation, Motor impairment, Rehabilitation, Behavioral tests, Positron emission tomography.

Motor impairments are among the major complications that develop after cortical damage caused by either stroke or traumatic brain injury. Motor cortex stimulation (MCS) can improve motor functions in animal models of stroke by inducing neuroplasticity. In the current study, the therapeutic effect of chronic MCS was assessed in a rat model of severe cortical damage. A controlled cortical impact (CCI) was applied to the forelimb area of the motor cortex followed by implantation of a flat electrode covering the lesion area. Forelimb function was assessed using the Montoya staircase test and the cylinder test before and after a period of chronic MCS. Furthermore, the effect of MCS on tissue metabolism and lesion size was measured using [^{18}F]-fluorodesoxyglucose (FDG) μPET scanning. CCI caused a considerable lesion at the level of the motor cortex and dorsal striatum together with a long-lasting behavioral phenotype of forelimb impairment. However, MCS applied to the CCI lesion did not lead to any improvement in limb functioning when compared to non-stimulated control rats. Also, MCS neither changed lesion size nor distribution of FDG. The current study questions the utility of MCS as a standalone treatment in a rat model of severe cortical damage.

#8512

Fornix Deep Brain Stimulation Induced Long-Term Spatial Memory Independent of Hippocampal Neurogenesis

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Keywords: Deep brain stimulation, Fornix, Hippocampus, Memory, Neurogenesis.

Deep brain stimulation (DBS) is an established symptomatic treatment modality for movement disorders and constitutes an emerging therapeutic approach for the treatment of memory impairment. In line with this, fornix DBS has shown to ameliorate cognitive decline associated with dementia. Nonetheless, mechanisms mediating clinical effects in demented patients or patients with other neurological disorders are largely unknown. There is evidence that DBS is able to modulate neurophysiological activity in targeted brain regions. We therefore hypothesized that DBS might be able to influence cognitive function via activity-dependent regulation of hippocampal neurogenesis. Using stimulation parameters, which were validated to restore memory loss in a previous behavioral study, we here assessed long-term effects of fornix DBS. To do so, we injected the thymidine analog, 5-bromo-2'-deoxyuridine (BrdU), after DBS and perfused the animals 6.5 weeks later. A week prior to perfusion, memory performance was assessed in the water maze. We found that acute stimulation of the fornix improved spatial memory performance in the water maze when the probe trial was performed 1 h after the last training session. However, no evidence for stimulation-induced neurogenesis was found in fornix DBS rats when compared to sham. Our results suggest that fornix DBS improves memory functions independent of hippocampal neurogenesis, possibly through other mechanisms such as synaptic plasticity and acute neurotransmitter release.

#8588

Effects Stimulation in the Nucleus Entopeduncularis on Neuronal Network Activity after Apomorphine-Induced Deficient Sensorimotor Gating in a Rat Model

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Keywords: Nucleus accumbens, Medial prefrontal cortex, Deep brain stimulation, Neuropsychiatric disorder.

Introduction: Deficient sensorimotor gating induced by dopamine receptor agonists is used as an endophenotype for certain neuropsychiatric disorders, such as Tourette's syndrome. Deep brain stimulation (DBS) of the globus pallidus internus (GPi) is experimentally used to alleviate tics in Tourette's syndrome. One operational measure of sensorimotor gating is prepulse inhibition (PPI) of the acoustic startle response (ASR). We recently showed that DBS of the rat nucleus entopeduncularis (EPN, the equivalent to the human GPi) alleviates an apomorphine induced PPI deficit. The aim of our study was to investigate the effects of stimulation in the EPN on single neuronal activity of the medial prefrontal cortex (mPFC) and the nucleus accumbens (NAC) and coherence of oscillatory activity with sensorimotor cortex.

Methods: Neuronal recordings were carried out in urethane anesthetized (1.4 g/kg, i.p.) male Sprague-Dawley rats. A concentric bipolar electrode for stimulation was stereotaxically implanted in the EPN. Single neuronal recordings were acquired from the mPFC and NAC before and after apomorphine injection (1 mg/kg BW). Thereafter, 60 sec EPN stimulation (130 Hz, 100 μA current, with 120 μs biphasic square wave pulses) was applied and the neuronal activity recorded.

Results: Neuronal firing rate was not affected by apomorphine injection in both regions, but enhanced after stimulation in the NAC. Measures of irregularity were enhanced after apomorphine injection in both regions. Stimulation normalized this measure in the NAC, but had no effect in the mPFC. Coherence of oscillatory theta (4–8 Hz) and alpha (8–12 Hz) band activity between the mPFC and NAC local field potentials and sensory motor cortical field potentials was enhanced after apomorphine injection. EPN stimulation reduced theta and alpha coherence in the NAC, while in the PFC only alpha activity was reduced.

Conclusion: These investigations shed new light on the effect of DBS on disturbed neuronal network activity in an animal model with sensorimotor gating deficit, which may be used to understand and improve this experimental therapy in neuropsychiatric disorders.

#8590

The Centromedian-Parafascicular Complex May Signal Behaviorally Relevant Events during Auditory Processing

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Keywords: Intracranial ERPs, CM-Pf, Attention.

The centromedian-parafascicular complex (CM-Pf) of the thalamus has been shown to be sensitive to behaviorally significant sensory events and plays an essential role in the process of attentional orienting to external events. We here investigated involvement of this region in processing of task relevant auditory information by simultaneous cortical and subcortical recordings in patients with chronic neuropathic pain during an auditory three-class oddball paradigm. This task typically produces a P3 component to relevant stimuli and is known to reflect attentional processes requiring stimulus detection and discrimination.

Simultaneous intracranial local field potentials (LFPs) and scalp electroencephalography (EEG) were obtained in 5 patients (1 female) implanted with quadripolar electrodes in the CM-Pf for deep brain stimulation (DBS). Within 5 days after surgery, patients performed the oddball paradigm with externalized DBS electrodes. Subcortical and cortical event-related potentials (ERPs) were analyzed upon presentation of one frequent standard stimulus (900 Hz; 72%) and two infrequent stimuli (600 Hz and 1200 Hz; 14%), either being a relevant or a distractor stimulus. Furthermore, on the basis of previous studies investigating saliency, we tested whether neural oscillations in the beta (15–30 Hz) frequency range were modulated as a function of stimulus relevance.

Analysis revealed high accuracy of 89.6% ± 5.7 SEM in all patients. Cortical recordings over parietal regions and subcortical recordings in the CM-Pf showed largest P3 responses after presentation of rare relevant stimuli. Interestingly, peak latencies in the CM-Pf occurred prior to the cortical response. In addition, the time-frequency analysis of the CM-Pf revealed that neural oscillations in the beta frequency range were enhanced for relevant stimuli.

These findings show attention-related modulation of higher-order cognitive functions at the CM-Pf and suggest that sensory events could be labelled within the beta frequency range as behaviourally relevant before being distributed to the cortex.

#8857

Behavioral and Histological Impact of Bilateral High Frequency Stimulation of the Medial Forebrain Bundle Following Partial Dopamine Lesions in a Rodent Model of Depression

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Keywords: Depression, Rat, Deep brain stimulation, Medial forebrain bundle, Dopamine.

Introduction: Medial forebrain bundle (MFB) DBS in major depressive disorder patients showed rapid and long-term reduction of symptoms. However, the mechanisms and neurobiological outcome of the stimulation are not known. The current study looked at the effect of MFB high frequency stimulation (HFS) in animals with bilateral dopamine depleting ventral tegmental area (VTA) lesions.

Methods: Male Flinders Sensitive Line (FSL) and Sprague-Dawley (SD) control rats received bilateral, partial dopamine depleting lesions via injection of 6-OHDA into nucleus accumbens, the terminal region for mesolimbic midbrain projections. Simultaneously, animals received desipramine to protect the noradrenergic pathway. Later, animals were implanted with bilateral microelectrodes into the MFB followed by continuous HFS for 3 weeks. Stimulation parameters were: 130 Hz, pulse width 100 μs, and mean current 290 μA. Behavior assessments, including ultrasonic vocalization (USV), were performed at various time points to determine the impact of mesolimbic dopamine depletion and the role of MFB-HFS.

Results: The FSL animals showed increased response to amphetamine suggesting super sensitivity of their dopamine receptors. However, histological assessment of the brains and the evaluation of the level of dopamine depletion has not yet been completed. Full molecular and behavior analysis will be presented at the conference.

Conclusions: Dysfunctional dopamine transmission has been implicated in the manifestation of depression, and there is growing evidence suggesting that the FSL animals also have an altered dopaminergic system. How dopamine depletion influences the impact of MFB HFS will shed light on the role of dopamine in depressive-like symptoms, and this will be presented at the ESSFN meeting.

#8859

Bilateral High Frequency Stimulation of the Medial Forebrain Bundle in the Flinders Sensitive Line Rodent Model of Depression

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Keywords: Depression, Rat, Deep brain stimulation, Medial forebrain bundle, Behavior.

Introduction: Flinders Sensitive Line (FSL) rats have been selectively bred over many generations based on the 'depressive-like' phenotype which have been shown to be sensitive to antidepressant medications. Physiological changes reported in the FSL model associated with clinical depression include decreased BDNF levels in the hippocampus, and reduced baseline levels of serotonin, dopamine and its metabolite DOPAC in the nucleus accumbens. Furthermore, detailed assessment of the temporal dynamics of the FSL's behavior have shown both transient and long-term behavioral symptoms that are relevant in clinical depression, such as weight changes, lack of motivation, increased anxiety or cognitive, learning and memory deficits. The current study examined the impact of bilateral, continuous and chronic High Frequency Stimulation (HFS) of the Medial Forebrain Bundle (MFB) in the FSL model.

Methods: Male FSL rats and aged matched Sprague-Dawley controls were used in the experiment. Baseline analysis was carried out on a battery of behavioral tests, followed by the implantation of bilateral, bipolar electrodes into the medial forebrain bundle. Stimulation parameters were: 130 Hz, pulse width 100 μs, and mean current 290 μA. Following continuous and chronic stimulation for 3 weeks, the animals were retested on the behavioral paradigms. At the end of the study, animals were perfused and prepared for histological analysis.

Results: The current study confirms that several of the early behavior deficits observed in the FSL animals are transient. However, MFB HFS in the FSL animals improved learning and memory performance in the Double-H maze task and increased explorative behavior in the Open Field paradigm. Analysis of stimulation dependent gene expression (D1 and D2) in the nucleus accumbens and autoradiography for changes in dopaminergic and serotonergic receptors will be reported at the meeting.

Conclusions: The data suggests that electrical stimulation of the MFB in a rodent model of depression can improve certain behavioral measurements, particularly linked to learning and explorative behaviors. The biological basis of the stimulation effect, in particular the impact on D1 and D2 receptor levels and gene expression, will be discussed in more detail at the meeting.

#8886

A Novel Method for Stereotactic Implantation Neurosurgery Based on Individual Rat Coordinates Derived from Preoperative CT Imaging Coregistered to a Stereotactic MR Atlas

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Keywords: Stereotactic neurosurgery, Animal research, Laboratory animals.

Introduction: As brain implants such as electrodes to record and stimulate neural tissue in laboratory animals are becoming more and more sophisticated, implantation methods have not evolved over the last century. Essentially, the current animal research stereotactic implantation technique consists of 4 steps: (1) acquisition of a set of stereotactic coordinates from a histological stereotactic animal brain atlas; (2) adaptation of the skull position of the individual animal to match the brain atlas position; (3) definition of the atlas origin in the individual animal; and (4) burr hole drilling and implantation at the coordinates as defined in step 1 from the origin defined in step 3.

Meanwhile, clinical stereotactic implantation techniques have evolved in different steps from a technique very similar to the one still used in animal research based on skull landmarks via adaptation of stereotactic coordinates obtained from a stereotactic atlas by landmarks visualized on ventriculography, CT and MR, to direct visualization of targets on MR imaging. As stereotactic neurosurgery in humans has moved away from the use of atlases toward purely individual-based surgical planning, implantation accuracy and clinical benefit have improved.

The introduction of similar techniques in animal stereotactic surgery with a similar increase in implantation accuracy could result in (1) a decrease in the number of laboratory animals needed; (2) a gain in research time as less surgeries and postoperative test would be needed to perform; and (3) a direct impact on the scientific results and conclusions drawn. Taking this all together, implementation of any of the advances made in clinical neurosurgery into animal neurosurgery could even also be time- and cost-effective.

We aim to assess the differences in accuracy, time and costs between the conventional method and a new technique based on individual CT registered to an in-house developed CT atlas for stereotactic implantation of electrodes into rat brains.

Material and Methods: In 289 g male Wistar (SD 7.8 g; n = 12) and 424 g male Sprague Dawley (SD 6.2; n = 12) rats, preoperative CT imaging was followed by stereotactic implantation of 2 electrodes (one in each hemisphere), randomly targeting 4 targets. One electrode was implanted using the conventional technique (skull-flat positioning using bregma and lambda, atlas-based coordinates with bregma as an origin), while the second electrode was implanted using a novel technique (skull-flat positioning using 2 individually chosen CT-based landmarks, atlas-based coor-

dinates recalculated from co-registration of the individual CT to an in-house developed CT atlas, with a third individually chosen CT-based landmark as an origin).

Next, the electrode tips were localized using ex vivo CT imaging with the skull and electrodes in place. The electrode tips were picked by a researcher who was blinded to the surgical method used.

Results: Offsets between the intended brain entry points/targets and the reached brain entry points/targets, respectively, were calculated in all 3 orthogonal planes. In Wistar rats, matching perfectly to the so-called 'atlas' rat used by Paxinos et al. for construction of a stereotactic atlas, the dorsoventral offset at target was significantly larger using the conventional technique vs. the novel technique (0.9 vs. 0.1 mm, $P < 0.05$). Similarly, in Sprague-Dawley rats, craniometrically differing from the 'atlas rat', the dorsoventral offset at target was significantly larger using the conventional technique vs. the novel technique (0.7 vs. 0.0 mm, $P < 0.05$). In the other orthogonal planes, the offsets did not differ significantly between the 2 techniques in both strains.

For CT acquisition, image processing, coregistration to the CT and MR atlas and landmark picking to obtain the final surgical coordinates, an additional time of 47 minutes per animal is needed in the novel technique as compared to the conventional technique. The surgical procedure itself is not prolonged when using the novel technique.

The cost for obtaining the pre-operative CT was 7.5 euros per rat in our institution.

Conclusion: While being more time-consuming and slightly more expensive, preoperative CT-based individualized stereotactic implantation surgery in rats could result in a higher implantation accuracy relative to the intended target. Hence, when high accuracy is needed, it might become time- and cost-effective, reduce the number of animals needed and increase research quality.

Movement Disorders

#7847

DBS and Parkinson's Disease – Two-Step Strategy

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Keywords: Functional, Parkinson's, DBS, Infection, Prevention, Protocol.

Introduction: Implant infection in DBS surgery is one feared complication. The growing number of DBS surgeries performed and use in a broader number of pathologies, may lead to a rising number of infections. There are no globally accepted guidelines for preventing this complication.

Methods: A cohort study was perfomed including all patients submitted to DBS surgery for Parkinson's disease during the time period ranging from 2006 to 2016. Our group adopted in 2010 a two-step surgery, dividing the long DBS surgery procedure into two shorter ones. Data was divided into early infections (occurring in the first 90 days) and late infections (after 90 days). Our primary outcome was the infection rate in both groups and secondary outcomes were early infection rate (≤90 days), late infection rate (>90 days), time-to-infection, infection per year, infection site and involved microorganism.

Results: Total population included 190 patients (61.58% (n = 117) males, 38.42% (n = 73) females), 40.5% (n = 77) in the 1-procedure group and 59.47% (n = 113) in the 2-procedure group. Considering our primary outcome, 8 infections were diagnosed in the 1-procedure group (infection rate of 8.2%) and 1 in the two-procedure group (infections rate of 0.54%) – p value = 0.041. Early infections were detected only in the 1-procedure group (2.1% – n = 4 – versus 0%, p-value = 0.033).

Conclusions: A standardized definition of surgical site infection and treatment guidelines are required. Our results indicate that splitting DBS surgery for Parkinson's into a two-phase surgery may actually decrease the rate of infection, as opposed to the classic procedure practiced in most centers.

#8279

An International, Randomized, Controlled Trial of Focused Ultrasound Thalamotomy for Essential Tremor

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Keywords: Focused ultrasound, Thalamotomy, Essential tremor.

Background: Recent advances in ultrasound transducer technology have allowed ultrasound to be transmitted with precision through the human skull. Pilot studies suggest that MR guided focused ultrasound can be used to successfully generate stereotactic thalamic lesions. We present the one year results of a double-blinded, randomized, controlled trial of FUS thalamotomy for essential tremor.

Methods: Seventy-six patients with medication-refractory essential tremor were randomized 3:1 to receive a unilateral focused ultrasound thalamotomy or a sham procedure. Tremor (CRST) and quality of life (QUEST) measures were obtained at baseline, 3, 6, and 12 months. Safety was determined adverse event

monitoring throughout the study. All tremor assessments were videotaped and then rated by an independent core lab of neurologists who not involved in the procedures.

Results: Contralateral hand tremor, the primary endpoint, was improved by 49% at 3 months ($p < 0.001$) with the treatment (18.09 +4.81 to 9.55 + 5.06) compared to sham procedures (16.00 + 4.42 to 15.75 + 4.90) and the effect was durable at one year (10.89+4.86). Similarly, functional measures of disability and quality of life were statistically improved whereas there was no change in the sham cohort. The most common side effects were paresthesia and gait disturbances, and remained at 12 months in 14% and 9%, respectively.

Conclusion: Focused ultrasound can be delivered effectively through the intact skull to make precise ablations deep in the brain. MR guided focused ultrasound thalamotomy improves hand tremor and quality of life in ET with an acceptable safety profile.

#8430

Prelemniscal Radiations Fiber Composition and DBS Induced Metabolic Activity in Parkinson's Disease

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Keywords: Raprl-Tractography, PET/CT, Parkinson's disease.

Objective: Prelemniscal radiations (Raprl) have been reported as a safe and effective target to treat the symptomatic triade of Parkinson's disease. However, little is known about the anatomical connectivity of its fibers and the mechanism of action of DBS in this area. The present report studies the fiber composition of Raprl through high resolution tractography and the effect of DBS on PET/CT metabolic activity of Regions of Interest (ROIs) derived from tractography.

Material and Methods: Twenty patients with prominent unilateral motor symptoms of PD were scanned with 3T MRI, in which diffusion weighted images (DWI) were acquired and constrained spherical deconvolution (CSD) identified diffusion profile in different directions. In five patients DBS electrodes were implanted in Raprl contralateral to most prominent symptoms and ^{18}Fluor-Deoxy- glucose (FDG) PET/CT performed preoperatively and after DBS was optimized. Metabolic changes induced by DBS on Regions of Interest (ROIs) derived from tractography, were determined by Statistical Parametric Mapping (SPM8). Non-stimulated hemisphere served as control for pre and post DBS PET/CT studies.

Results: In all cases tractography identified three major components: 1. Cerebellar-Thalamic-Cortical component, that at the level of the thalamus and cortex segregated in a posterior subset connecting with Vim and Primary Motor Cortex (PMC), and anterior subset connecting with the Vop and Supplementary Motor Cortex (SMC). 2. A component connecting Gpi through ansa lenticularis with the sub thalamus, were it divided into a superior subset to overlap cerebellar fibers in Vop and a subset continuing through Raprl to the dorsal brain stem between medial lemniscus and brachium conjunctivum, probably PPN 3. Fibers connecting orbital and dorsolateral frontal cortices with the mesencephalic tegmentum. On the other hand, Raprl-DBS induced an improvement >80% of symptoms, which correlated with a highly significant decrease of metabolic activity in PMC, SMA, Raprl, VL Thalamus, and both cerebellar hemispheres.

Conclusion: Raprl connectivity explains the effect of DBS on PD motor symptoms. Contrary to the current hypothesis of PD physiopathology, DBS induced a significant inhibition of Raprl that extends downstream to VL thalamus, motor cortices and cerebellum, associated with significant improvement of motor symptoms of PD.

#8438

The Effect of Unilateral Thalamic Deep Brain Stimulation on the Vocal Dysfunction of a Patient with Spasmodic Dysphonia: A Prospective, Randomized, Double-Blinded Assessment

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Keywords: Spasmodic Dysphonia, Dystonia, Deep Brain Stimulation.

Introduction: Spasmodic dysphonia (SD) is a neurological disorder of the voice where a patient's ability to speak is compromised due to involuntary contractions of the intrinsic laryngeal muscles. Since the 1980s, SD has been treated with Botulinum Toxin A (BTX) injections into the throat. This therapy is limited by the delayed-onset of benefits, wearing-off effects, and repeated injections required every three months. In a patient with essential tremor (ET) and coincident SD, we set out to quantify the effects of thalamic Deep Brain Stimulation (DBS) on vocal function while investigating the underlying motor thalamic circuitry.

Methods: The University of British Columbia Clinical Research Ethics Board approved this study (H14-03192). A 79-year old right-handed woman with ET and coincident adductor SD was referred to our neurosurgical team. While primarily treating her limb tremor, we studied the effects of unilateral, thalamic DBS on vocal function using the Unified Spasmodic Dysphonia Rating Scale (USDRS) and Voice-Related Quality of Life (Vr-QoL). Since dystonia is increasingly being considered a multi-nodal network disorder, an anterior trajectory into the left thalamus was deliberately chosen such that the proximal contacts of the electrode were in the Voa nucleus (pallidal outflow) and the distal contacts were in the Vim nucleus (cerebellar outflow). In addition to assessing ON/OFF unilateral thalamic Vim stimulation on voice, we experimentally assessed low voltage unilateral Vim, Voa, or multi-target stimulation in a prospective, randomized, doubled-blinded manner. Evaluators were experienced at rating SD and were familiar with the vocal tremor of ET. A Wilcoxon Signed-Rank test was used to study the pre- and post-treatment effect of DBS on voice.

Results: Unilateral left thalamic Vim stimulation (DBS ON) significantly improved SD vocal dysfunction compared to no stimulation (DBS OFF) as measured by the USDRS ($p < 0.01$) and Vr-QoL ($p < 0.01$). Audio 1 and Audio 2 respectively highlight DBS OFF vs. DBS ON of the SD voice. In our experimental interrogation, both low voltage Vim ($p < 0.01$) and multi-target Vim+ Voa ($p < 0.01$) stimulation were significantly superior to low voltage Voa stimulation.

Discussion: The coordination of speech production is facilitated by the cerebellar motor input to the laryngeal motor cortex via the motor thalamus. This neural circuit controls the timing between single components of a movement, scales the size of muscular action, and coordinates the sequence of agonists and antagonists in normal speech production. While the basal ganglia undoubtedly plays an important role in limb, axial, and facial dystonia (including tongue), it appears that principally treating cerebellar dysfunction is required to correct abnormal speech coordination in SD. Multiple neuroimaging and physiological studies of focal dystonia point towards significant cerebellar dysfunction. This study is limited by the USDRS (and other adductor SD severity scales), which is conducted under non-stressful conditions and do not mimic real life stressful conditions; our patient reported even more profound benefits in real life situations. Second, the DBS settings were programmed to maximally alleviate limb tremor and perhaps further optimization can be achieved for voice. Our patient improved from unintelligible to easily understandable speech following a single DBS lead. Further incremental improvements in voice following contralateral surgery (if true) may not warrant the additional risks.

Conclusion: For the first time, the effects of high-frequency stimulation of different neural circuits in SD have been quantified. Unexpectedly, focused Voa (pallidal outflow) stimulation was inferior to Vim (cerebellar outflow) stimulation despite SD's classification as a dystonia. While only a single case, scattered reports exist on the positive effects of thalamic DBS on dysphonia. A Phase 1 pilot trial (DEBUSSY) is underway at our centre to evaluate the safety and preliminary efficacy of DBS in SD. We hope this work stimulates neurosurgeons to investigate this new indication for DBS.

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#8445

Stereotactic Lesional Interventions for Parkinson's Disease: An Experience of 465 Patients

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Keywords: Parkinson's disease, Stereotactic thalamotomy, pallidotomy, Subthalamotomy.

Objectives: Parkinson's disease (PD) is one of the most widespread progressive neurodegenerative diseases, which in most cases has bilateral clinical signs. DBS for PD is a proven technology that significantly improves motor function, reduces disability of patients suffering from the adverse effects of L-dopa therapy. Meanwhile the application of ablative surgical procedures remains important in the treatment of extrapyramidal movement disorders in view of economical, geographical and some other reasons. The purpose of the study is to evaluate the effectiveness of stereotactic lesion procedures for PD.

Methods: 465 patients with PD underwent stereotactic ablative surgery from 2011 to 2015. Among them unilateral thalamotomy performed in 422 (90.8%) cases, unilateral pallidotomy – in 22 (4.7%) cases, thalamotomy and contralateral pallidotomy at 20 (4.2%) cases, thalamotomy and contralateral subthalamotomy at 10 (2.1%) cases and bilateral pallidotomy at 1 (0.2%) case. Neurological and psychological status assessed by: UPDRS II, Hoehn and Yahr scale, Schwab and England scale, MMSE, Beck's Depression Inventory, Hamilton Depression Rating Scale, Hamilton Anxiety Rating Scale and PDQ-39. Surgery performed on CRW Stereotactic system using StereoPlan, StereoAtlas (Radionics) and FrameLink (Medtronic) softwares. Intraoperative macrostimulation was used to delineate the optimal target location. Postoperative follow-up was from 6 months to 8 years (mean 4.8 ± 0.5 years).

Results: Patient's age ranged from 30 to 84 years (mean – 58.8 years). Mean disease duration before surgery was 9.9 years. L-dopa therapy used 394 (85%) patients with mean dose 780.4 mg/day. Mean duration of L-dopa therapy was 5.5 years, 172 (43.7%) of them had motor fluctuations and/or levodopa-induced dyskinesia. Overall regression of tremor observed in 85% patients, rigidity – in 88%, bradykinesia – in 59% patients. In 1 year after the intervention UPDRS score improved by 52% in ON period and by 41% in OFF period. The dose of levodopa decreased in average on 33% – from 780.4 mg/day to 522.7 mg/day. After treatment Schwab and England score increased from to 56.7% to 80.6%. Surgical complications, which include hemorrhage, local ischemia, infection and pulmonary embolism were observed in 15 (3.1%) patients. Neurological complications have happened in 26 patients (5.5%), in most cases they were combined and include speech disturbances – 10 (2.1%), pseudobulbar palsy – 1 (0.2%), gait disturbances – 6 (1.3%), hemiballism – 2 (0.4%), memory disturbances and cognitive impairment – 12 (2.6%), syndrome of vegetative irritation – 4 (0.8%), contralateral dyspraxia – 2 (0.4%). Postoperative mortality rate was 0.4% (one patient dead after pulmonary embolism and second – after intracerebral hemorrhage).

Conclusion: Our results demonstrate that ablative surgery is effective and safe method of treatment for PD. Such treatment improves overall motor function, increased patient's mobility, daily living activities and improves quality of life. Stereotactic lesion interventions allow patients to reduce levodopa dose, providing them with increased freedom from a complex medication regimen. The best candidates for ablative surgery include patients with tremor, rigidity, L-dopa induced dyskinesia and minimal bradykinesia. Poor prognostic factors for lesion intervention in patients with PD include arterial hypertension, hydrocephalus, atherosclerotic microangiopathy and diabetes. Careful identification and selection of patients for ablative surgery allows to achieve optimal results in the treatment of PD.

#8451

MRI Guided High Intensity Focused Ultrasond for the Treatment of Essential Tremor: Clinical Outcome and Radiological Findings of Unilateral Thalamotomy

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Keywords: Essential tremor, Thalamotomy, Focused ultrasound.

Objective: To report the preliminar clinical experience in our center (CINAC-HM Puerta del Sur) in the treatment of essential (ET) with MRI guided High-Intensity Focused Ultrasound (MRgHIFU).

Background: Ablative neurosurgery for the treatment of movement disorders such as ET has been performed for decades. However, after the appearance of Deep brain stimulation in the late 80's, lesional strategies were practically relegated. The recent development of the non-surgical low-invasive MRgHIFU has paved the way for the rebirth of ablative approaches for the treatment of Movement Disorders.

Methods: From July 2015 to February 2016 twelve ET patients underwent unilateral thermal thalamotomy with MRgHIFU. Tremor severity was assessed with the Clinical Rating Scale for Tremor (CRST) in all patients at baseline and 3 month after treatment. A visual analogue scale for the assessment of overall quality of life (ranging from 0 to 100% with higher scores indicating better perceived quality of life) was also given pretreatment and after procedure. Treatment-related adverse events were also registered. Topographic radiologic analysis of the lesions was performed.

Results: Total CRST score showed an improvement mean reduction of 56% ($p < 0.00001$). Furthermore, scores for tremor corresponding to the treated hemibody were reduced from to 74% ($p < 0.00001$). The part C of the CRST evaluating disability in activities of daily living improved from to 75% ($p < 0.00001$). The VAS improved from 44% at baseline to 77% ($p < 0.00001$).

During the procedure, all patients complaint of nausea and/or headache with different degrees of severity, in one case it resulted in incomplete sonication. The most frequent postreatment adverse event was gait unstability and ipsilateral limb ataxia (5 patients) which progressively improved in the follow-up (only in one patient persisted 3 months after treatment). Three patients reported mild bucal paresthesias that persisted 3 months after treatment.

Medium volume size lesion was 64.9 mm3 (8.1 x 4 x 7.2 mm) and location was 14.8 mm lateral from AC-PC and 8.2 anterior from PC. We found a positive correlation between tremor improvement and percentage of Vim lesioned.

Conclusion: This pilot study supports previous evidence showing that MRgHIFU is safe and effective for the treatment of ET tremor and results in huge reduction of daily living disability. Larger, controlled and randomized trials are mandatory to confirm these findings.

#8456

A Comparison of Outcomes between Deep Brain Stimulation (DBS) Under General Anesthesia versus Conscious Sedation with Awake Evaluation

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Keywords: Deep brain stimulation (DBS), Subthalamic nucleus, STN, STN-DBS, Anesthesia, Sedation, Parkinson's disease.

Introduction: Deep Brain Stimulation (DBS) of the subthalamic nucleus (STN) is considered safe and effective for the management of motor symptoms of Parkinson's disease (PD). DBS is typically performed under conscious sedation with awake evaluation during intraoperative testing (Machado *et al*., 2012). However, recent developments in surgical techniques allow for subjects to be asleep during the DBS procedure using general anesthesia. Previously reported long term outcomes of subjects who underwent STN-DBS under general anesthesia demonstrated postoperative safety and efficacy up to 1 year (Harries *et al*., 2012). We report the outcomes of subjects undergoing STN-DBS procedure with general anesthesia or conscious sedation with awake evaluation up to 1 year post-lead placement, as part of the ongoing VANTAGE Clinical Study.

Methods: VANTAGE is a prospective, multi-center, non-randomized, open-label interventional trial, sponsored by Boston Scientific Corporation. The trial assesses motor improvement in subjects with moderate-to-severe PD following bilateral STN-DBS.

Assessments include Unified Parkinson's Disease Rating Scale (UPDRS), Parkinson's Disease Questionnaire (PDQ-39), Modified Schwab and England (SE), and Global Impression of Change. Change in anti-parkinsonian medication was also documented. Forty subjects were implanted bilaterally with the Vercise DBS System (Boston Scientific Corporation) at 6 European centers. Of these, 19 (47%) underwent the DBS procedure under general anesthesia.

Results: A consistent trend was observed of subjects undergoing general anesthesia reporting an improvement in their motor function similar to those who underwent DBS with conscious sedation and awake evaluation (versus baseline). No statistical significant difference was found in motor function between general anesthesia versus conscious sedation with awake evaluation, although this could be due to the small sample size in each group in this cohort.

Conclusions: This data suggests that providing surgical options to patients, with regard to using general anesthesia versus conscious sedation with awake evaluation during the DBS procedure, has no significant effect on subsequent clinical outcomes up to 1 year post-implant.

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#8457

Outcomes of a Prospective, Multi-Center International Registry of DBS for Parkinson's Disease

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Keywords: Deep brain stimulation (DBS), Subthalamic nucleus, STN, STN-DBS, Parkinson's disease, Registry, Clinical trial.

Introduction: The effectiveness and safety of the use of Deep Brain Stimulation (DBS) to reduce motor complications of subjects with Parkinson's disease (PD) has been substantiated by several randomized controlled trials (Deuschl et al., 2006, Weaver et al., 2009, Okun et al., 2012, Scheupbach et al., 2013). Motor improvement following DBS is sustained for up to 10 years as reported by Castrioto et al. An in-depth evaluation of real-world outcomes following DBS will add to the existing database of knowledge and prove to be a useful tool for physicians. We present the outcomes of a large scale clinical registry that compiles the effectiveness and safety-related real-world outcomes of a multiple-source, constant-current DBS System in the treatment of levodopa-responsive PD.

Methods: The Vercise DBS Registry is a prospective, on-label, multi-center, international registry sponsored by Boston Scientific Corporation. The Vercise DBS system (Boston Scientific) is a CE-marked, multiple-source, constant-current system with a rechargeable battery. Subjects will be followed up at 3, 6.12 months and up to 3 years post-implantation where their overall improvement in quality of life and PD motor symptoms will be evaluated. Clinical endpoints will be evaluated at baseline and during study follow up that include Unified Parkinson's Disease Rating Scale (UPDRS), MDS-UPDRS, Parkinson's disease Questionnaire (PDQ-39), and Global Impression of Change. The registry also utilizes the newly developed MDS UPDRS for the evaluation of motor symptoms and includes the evaluation of non-motor symptoms of PD (Non-Motor Symptom Assessment Scale) following DBS. Adverse events are also collected.

Results: This report will provide the safety and effectiveness outcomes of the first cohort of subjects implanted with the Vercise DBS System analyzed at 6 months post-implantation as compared with baseline.

Discussion: The Vercise DBS registry study represents the first comprehensive, large scale collection of real-world outcomes and evaluation of the safety and effectiveness of the Vercise DBS System. This report will provide such data from the first cohort of subjects analyzed at 6 months post-implantation as compared with baseline.

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#8461

High Cervical Spinal Cord Stimulation (HCSCS) May Improve the Motor Symptoms in Parkinson's Disease

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Keywords: Spinal Cord Stimulation (SCS) – burst mode – motor synmptoms – PD.

Introduction: There is evidence that High Cervical Spinal Cord Stimulation (HCSCS) may control motor symptoms in Parkinson Disease (PD). In this work we evaluated follow-up results of HCSCS in PD, also considering recent advances of available stimulating devices.

Methods: Twelve male patients (age 63 ± 10.3, disease duration 10 ± 2.3 years) showing tremor, rigidity, gait and posture disturbances were studied. Leg pain affected 5 out of the 12 patients. Patients selection was based on advanced age, presence of general diseases and/or exclusion of STN or PPTg DBS. HCSCS was applied via a percutaneous quadripolar lead (4/12) (Medtronic 3487A, USA) or an octapolar lead (8/12) (St. Jude, USA). Continuous stimulation was used in 4 patients (Synergy Versitrel, Medtronic, USA), while burst stimulation was applied in the others (Prodigy, St. Jude, USA). UPDRS III, sub-items 27–30 and H&Y scales were evaluated to assess clinical output; videos, static posturometric and gait analysis allowed objective evaluations in different stimulation setups and repeated after 3 and 6 months.

Results: No surgical complications occurred. Pain was quickly reduced, both under continuous and burst stimulation, with consistent reduction of analgesic drugs. The major effects of HCSCS on PD symptoms were a restoring of gait and motor abilities and, surprisingly, a control of tremor, especially when the burst mode was applied.

Conclusions: The effectiveness on PD motor disabilities shows that HCSCS is promising. In our initial experience, using continuous HCSCS, immediate benefits were not evident since influenced by paresthesias. However, long-lasting effects provided convincing clinical evidence about effectiveness on pain as well as PD symptoms. The successful of this therapy was more pronounced with burst stimulation and clearly ameliorated QoL. Given these promising data, we are planning to apply HCSCS in a larger group of PD patients, who in the past were considered to be not eligible for classic DBS.

#8472

Once DBS, Always DBS? – Clinical, Ethical, and Financial Considerations Related to DBS

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Keywords: DBS, Withdrawal syndrome, Ablative surgery.

Background: Deep Brain Stimulation (DBS) has become a popular method for treatment of patients with advanced Parkinson's disease (PD) and dystonia, and increasingly used for neuropsychiatric conditions. DBS is advertised as reversible and adaptable, as opposed to stereotactic lesions, which are described as permanent and irreversible. However, little is known about the issue of patients becoming 'addicted' to DBS, especially DBS of the subthalamic nucleus (STN) in PD, and pallidal DBS in dystonia. DBS hardware can become infected, necessitating its removal and the patient cannot be re-implanted until infection is cleared which can take time. Also, DBS requires regular replacements of the implanted pulse generator (IPG), which is very costly and involves a new surgical procedure every 1–5 years (depending on diagnosis), with increased risk for infection. In case of withdrawal of DBS, either due to infection or due to inability for patients to pay for a new IPG, a 'DBS withdrawal syndrome' or rebound of symptoms can develop: it can be a malignant parkinsonian crisis that may be refractory to intensive medical treatment and includes akinetic crisis with hyperthermia and rhabdomyolysis that may lead to renal failure and eventually death. It can also be a dystonic storm requesting intensive care with also risk for rhabdomyolysis and death. It can be a full blown rebound of a psychiatric condition that may lead to suicide. These issues are seldom discussed in the DBS narratives.

Objective: To review the literature and own experience about the occurrence of a 'DBS withdrawal syndrome', and ponder the ethical and financial issues when advising patients about a surgical procedure that will entail life-long maintenance and recurring high financial costs. To discuss the role of, and need for, stereotactic ablative surgery in these conditions.

Material and Method: A search of PubMed using the words 'deep brain stimulation' and 'withdrawal' was conducted. A review of own and others' experience was gathered.

Results: Only three peer-reviewed publications were found describing a total of 6 patients in whom cessation of STN DBS led to a severe medication-refractory malignant parkinsonian syndrome, leading to death in three of them. Other cases of symptom rebound after DBS have been reported anecdotally. Own and others' experience revealed also cases where rebound and withdrawal syndrome occurred in patients who had been on DBS for dystonia and PD, as well as for OCD and depression.

Conclusion: Patients considered for DBS should be informed that they may become dependent on a device that will need regular checks and replacements, and which they may not afford in the long run, unless it is reimbursed by insurance or by the Healthcare system. Rechargeable stimulator may be a solution but these are expensive and not free from becoming infected and explanted, leading to same problem of rebound. Upon abrupt cessation of DBS, a severe potentially fatal withdrawal syndrome may occur despite intensive medical treatment. In these instances, a

stereotactic lesioning procedure (pallidotomy, subthalamotomy, capsulotomy, cingulotomy) may be considered and may be in fact lifesaving. There is a need to maintain and expand training and skills of functional neurosurgeons in performing stereotactic neurosurgical ablative procedures.

#8510

Safety of STN Gamma Knife Radiosurgery for Parkinson's Disease: Preliminary Results of a Prospective Study

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Keywords: Trial movement disorder.

Background: Chronic STN stimulation is an established treatment for complicated PD. Bilateral subthalamotomy may induce significant and long-lasting results when DBS is not available. We organized a prospective multicentric phase III trial (N° 2009-AO1227-50-MS1) in order to assess the safety of Gamma Knife radiosurgery (GKS) in this indication.

Methods: Between February 2011 & December 2013 were included and operated 14 patients at Timone University Hospital. All were presenting with PD at the stage of severe motor complications, were fullfilling criterion for STN DBS with a major contraindication for DBS. Each patient gave his informed consent. The GKS dose at the maximum was 110 Grays (1 isocenter of 4 mm). The STN contralateral to the most affected side was treated first. The mediane age was 66 years (56–72).

Results: Five patients got the other side treated at 12–15 months. One patient got the other side treated at 18 months and one other at 24 months. One patient completed is FU with only one side treated due to the good efficacy and the absence of extrapyramidal signs on the other side. 13 severe adverse events were reported. One patient died of unrelated cause at 6 months (he reported slight motor improvement at 3 months) and one comitted suicide at 6 months and one got an hospital stay for adaptation of the medical treatment. MRI showed typical ring-enhancing lesion. Till now, 2 patients presented MR hyperrespons. One got a dystonic foot for some months and one got non motor hyperdopaminergic signs improved after Dopa-agonist reduction. We observed no permanent neurological complication no neuropsychological worsening.

Conclusion: These preliminary results show that GKS of the STN is feasible with excellent safety in patients with severe PD. Efficacy seems promizing but still under evaluation. It may be an alternative treatment in case of contraindication for STN DBS. Longer follow up and larger prospective cohorte are needed for further confirmation of these preliminary results.

#8522

Three Year Outcomes of a Prospective, Multi-Center Trial Evaluating Deep Brain Stimulation with a New Multiple-Source, Constant-Current Rechargeable System in Parkinson's Disease

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Keywords: Deep brain stimulation (DBS), Subthalamic nucleus, STN, STN-DBS, Parkinson's disease, Constant current, Clinical trial, Rechargeable.

Introduction: Deep Brain stimulation (DBS) of the subthalamic nucleus (STN) is an established therapeutic option for patients with advanced Parkinson's disease (PD), supported by several randomized controlled trials. A device that enables fractionalisation of current using a multiple-source mode of delivery can permit the application of a well-defined, shaped electrical field. Thus, we postulated that a multiple-source, constant-current device (CE marked) that permits a well-defined distribution of current would lead to motor improvement in patients with Parkinson's disease. Previously, we reported results from the VANTAGE clinical study demonstrating highly significant improved motor function ($p < 0.0001$) as assessed by UPDRS III 'meds off' at 6 months post-first lead implant as compared with Baseline 'meds off,' thereby successfully achieving the study primary endpoint. In this report, we now present the three year, long-term follow up results of patients in the VANTAGE clinical study that employed multiple independent current control (MICC) DBS in the management of symptoms of Parkinson's disease.

Methods and Materials: VANTAGE is a monitored, prospective, multi-center, non-randomized, open-label interventional trial sponsored by Boston Scientific Corporation. Forty subjects with idiopathic Parkinson's disease (PD) were implanted bilaterally with a DBS system (Vercise) targeting the STN and followed up to three years post-lead placement. Assessments measured up to 3 years post-lead placement included the following: Levodopa Equivalent Dose (LED), Parkinson's Disease Questionnaire (PDQ-39), Global Impression of Change, and Modified Schwab and England (SE) scores. Adverse events were also recorded.

Results: Anti-parkinsonian medications as measured by LED remain stable up to 3 years post-lead placement (average of 1399 mg at baseline versus average of 699 mg at 3 years post-implant). PDQ-39 summary index scores demonstrate continued improvement in quality of life at 3 years post-lead placement on the basis of the following: bodily discomfort and activity of daily living measurements achieved statistical significance (p values of 0.001, 0.0173, respectively), sustained improvement of mobility

and emotional well-being, stability of cognition with baseline values. Further, a high proportion of Global Impression of Change responses were characterized as 'improved' (Clinician: 88.2%; Subject: 82.4%) and modified Schwab and England scores remained stable up to 3 years post-lead placement.

Conclusion: The VANTAGE trial is the first reported trial of a multiple-source, constant-current rechargeable system for use in the management of PD symptoms. At year 3 post-lead implantation, medication usage, quality of life outcomes (including PDQ-39), and Schwab England Scale remain stable. The collected outcomes from this study will inform clinicians on the use of this system, and its flexibility to manage the symptoms of idiopathic Parkinson's disease.

#8523

DBS Electrode Implantation of the Posterior Subthalamic Area for Treatment of Essential Tremor: Proposal of MRI-Based Anatomical Landmarks

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Keywords: DBS, Essential tremor, DRTT.

Backgorund: Deep Brain Stimulation (DBS) is an approved treatment option for therapy of refractory essential tremor (ET). Although evidence exists about its therapeutic effect, the optimal location of stimulation to improve tremor is still a matter of debate. Apart from the Ventral Intermediate Thalamus (VIM), the posterior subthalamic area (PSA) including the Dentato-Rubro-Thalamic-Tract (DRTT) has more recently been proposed as an appropriate target. The objective of our study is to present our MRI-based targeting procedure and correlate it with the stimulation site, clinical outcome and DTI-based fiber tracking identification of the DRTT.

Methods: We present a prospective series of 9 patients with unilateral or bilateral DBS implantation in the PSA. T2-weighted MRI was used to target the PSA on axial slices 2–3 mm below mid-commissural point (MCP) within the white matter between red nucleus and subthalamic nucleus using iPlan Net 3.0 (BrainLab). Fiber tracking of the DRTT was performed in each patient. Stimulation site was obtained by calculation of the position of the active contact and its corresponding Volume of Tissue Activated (VTA). Active contact positions and VTA were correlated to clinical outcome.

Results: The mean position of the active contact was LAT 10.54; AP –3.80 and VERT –1.59 mm with reference to MCP. Projection of the mean active contact position and its corresponding VTA onto the Morel stereotactic atlas revealed a stimulation site within the PSA in the proximity of the DRTT. This was correlated with DTI fibertracking findings. DBS resulted in significant tremor reduction 3–6 months postoperatively on the Fahn–Tolosa–Marin Tremor Rating Scale (TRS).

Conclusions: DBS of the PSA is effective in the treatment of ET. Our MRI-based anatomical landmarks seem to be reliable to target the PSA in each individual case. Our DTI findings suggest that the DRTT is involved in the efficacy of PSA DBS, although DRTT is not clearly identifiable in each patient.

#8524

Spinal Cord Stimulation Improves Gait in Patients with Parkinson's Disease Previously Treated with Subthalamic Nucleus Deep Brain Stimulation

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Keywords: Parkinson's disease, Locomotion, Postural instability and gait disorder.

Introduction: Dopaminergic medications and deep brain stimulation (DBS) are well-established treatments for controlling motor symptoms and improving quality of life in Parkinson's disease (PD) (Cury et al., 2014; Odekerken et al., 2013). While these therapies ameliorate cardinal motor symptoms, their effects on postural instability and gait disturbance (PIGD) are not sustained at long-term (Ferraye et al., 2008). At present, the treatment of PD patients who continue to experience PIGD even after optimized medical therapy and DBS is considered quite challenging. This is of importance as falls associated with postural instability (Bloem, Grimbergen, et al., 2001) and gait disturbance are major sources of morbidity and mortality in advanced PD (Matinolli et al., 2011).

In rodent (Fuentes et al., 2009) and non-human primate PD models, (Santana et al., 2014) electrical stimulation of the spinal cord has been shown to improve locomotor activity and disrupt pathological neuronal oscillations in multiple basal ganglia structures. In humans, initial results of open label studies investigating the effectiveness of SCS in PD have been mixed. While one initial study did not demonstrate efficacy, (Thevathasan et al., 2010) recent reports have shown an improvement in both motor symptoms and gait (Agari and Date, 2012; Fénelon et al., 2012; Hassan et al., 2013; Landi et al., 2013). Possible reasons for such discrepancies include patient selection, the spinal level of electrode implantation (e.g. thoracic vs. cervical) and a placebo effect.

We conduct a phase 1 clinical trial to study the safety and efficacy of SCS on PIGD in four patients with advanced PD previously treated with subthalamic nucleus (STN) DBS. To mimic preclinical studies, high frequency SCS (300 Hz) was delivered through electrodes implanted in the upper thoracic spine. We found that this treatment improved gait measures, PD motor symptoms and quality of life in all four individuals. To further confirm these findings, patients receiving SCS at either 300 Hz or 60 Hz underwent blinded experiments to measure gait function. Despite perceiving similar paresthesias, objective improvements in gait were only observed at 300 Hz.

Methods: Patients.

The study was conducted from June 2014 to March 2015 in the Division of Functional Neurosurgery of the Hospital das Clínicas, University of São Paulo. It was approved by the local Ethics Committee (CAPPESQ-HCFMUSP #12690213.0.0000.0068) and registered at ClinicalTrials.gov (NCT02388204). All patients provided signed informed consent.

Subjects were recruited from our multidisciplinary DBS center. Before inclusion in the trial, patients underwent a routine therapeutic program to optimize physiotherapy, medication intake and DBS programming. Despite adequate motor control, they still exhibited severe postural instability and gait disturbance, which were considered as problematic and major contributors to a poor quality of life.

Inclusion criteria were twofold: 1) Presence of advanced idiopathic PD; 2) Significant PIGD despite optimized treatment with medications and bilateral STN DBS. During the study, the levodopa dose was not significantly altered.

Exclusion criteria were the presence of 1) dementia, active psychiatric symptoms, apathy, and/or behavioural disturbances and 2) medical conditions that precluded patients from undergoing spinal cord stimulation.

Surgery and Stimulation Parameters: The SCS system selected for this study automatically adjusted current amplitude according to position (i.e. increasing stimulation intensity when the patients stood up and decreasing it when they were laying supine). Paddle stimulating electrodes with three columns of 5, 6 and 5 contacts (5-6-5 Model 39565; Medtronic Inc., Minneapolis, MN, USA) were implanted under general anesthesia. After a small exposure of the interlaminar space, the ligamentum flavum was removed and the electrode placed in the epidural space covering the upper levels of the thoracic cord (T2 to T4). In a second procedure, electrodes were connected to a rechargeable pulse generator (Model 37714, Medtronic Inc.) implanted in the subcutaneous tissue of the upper buttock. Initial programming sessions were carried out 3–4 weeks later. To mimic preclinical experiments, (Fuentes et al., 2009; Santana et al., 2014) stimulation frequency and pulse width were set at 300 Hz and 90 μsec, respectively. Current amplitude was programmed at 105% of the sensory thresholds in the upright and supine positions.

Study Design and Outcomes: Locomotion and gait measurements were recorded serially at baseline, 1, 3, and 6 months after SCS using the following tests: 1) Timed up and go test (TUG): (Huang et al., 2011). Time in seconds required for patients to rise from a chair, walk 3 meters and return. The test was performed 3 times and the average value was considered for analysis. 2) Timed up and go test with dual task (TUG-DT): (Brauer et al., 2011) Patients had to do a verbal fluency test during the TUG. 3) 20 Meters Walking Test: (Combs et al., 2014) Time in seconds and number of steps required to walk a 20 m path (10 m to go and 10 m to return). 4) 20 Meters Walking Test with obstacles: (Bloem, Valkenburg, et al., 2001) Same as above with obstacles placed along the path. The test was performed twice. First, the patient had to walk over the obstacle and then around it. 4) Stride length: Estimated by calculating the ratio between the average number of steps and distance during the 20 meters test. During the 6th-month evaluation, testing was conducted 'ON' and 'OFF' medications (one week apart). In the latter, drugs were discontinued for at least 12 h. As no major differences in gait were noticed with or without medication intake (supplementary fig. 1), in the main text we only report 'OFF' drug outcome. To avoid severe 'OFF' periods, gait analyses were always carried out while patients were receiving DBS.

Secondary outcomes were defined as changes in quality of life, motor scales and balance recorded at 6 months post-surgery as compared to preoperative baseline. These variables were evaluated using the: 1) the Parkinson Disease Questionnaire 39 (PDQ-39), (Souza et al., 2007) 2) the Unified Parkinson's Disease Rating Scale motor scores (UPDRS III), 3) the Berg Balance scale (BBS), (Scalzo et al., 2009) and 4) The Freezing of Gait Questionnaire (FOG-Q) at base line and after 6 months (Giladi et al., 2009).

In addition to primary and secondary outcomes, patients were blindly assessed on the TUG and 20 meters walking test during a single session in the beginning of postoperative month 4. As subjects always noticed SCS-induced paresthesias, we have decided not to conduct regular 'on/off stimulation' evaluations. Instead, we recorded their performance using two different stimulation frequencies (60 Hz and 300 Hz), which elicited paresthesias that were equally perceived by the patients. On the day of testing, patients were brought back to the clinic with their SCS system turned off for at least 6 h and medications discontinued for at least 12 h. As no major differences in gait were noticed with or without medications in open label evaluations carried out at 1 and 3 months (supplementary fig. 1), blinded assessments were only conducted in the 'OFF' medication condition. Initial evaluations were recorded with the SCS OFF. After this baseline measurement, patients were randomly assigned to receive stimulation at 60 or 300 Hz (i.e. 2 patients each). Following an initial round of testing, SCS was turned off for 2 h. Thereafter, new assessments were carried out using the alternative frequency.

Data Analysis and Statistics: Variables were measured at baseline, 1, 3 and 6 months following SCS onset. Comparisons were conducted using repeated measures ANOVA (Bonferroni post hoc) or the Paired Samples Test. Effect size was calculated using $\omega 2$. All results were presented as percentage of baseline. Significance was set at $p \leq 0.05$. Values for individual patients are reported in supplementary tables 1 and 2.

Results: Four patients with advanced PD were included in this study. Average improvement after bilateral DBS without medication was 58% at 1 year. After 7.8 years, clinical improvement was reduced to 37%. Despite an adequate control of motor symptoms, all patients experienced a significant decrease in quality of life due to prominent PIGD.

Surgical procedures for implanting SCS electrodes were uneventful. Stimulation was delivered around the T2 spinal cord segment with outer contacts selected as anodes and inner contacts as cathodes. In the upright and supine positions, stimulation amplitude was set at 105% of the sensory threshold for paresthesias (4.6 ± 1.9 V while patients were standing and 2.0 ± 0.5 V while recumbent). At these voltages, SCS delivered at 300 Hz, (90 μsec pulse width) induced paresthesias that were relatively constant, did not produce any discomfort and did not change in intensity with the patient's position.

Primary Outcomes: All patients exhibited significant improvements in gait while receiving SCS in the 'ON' DBS 'OFF' Meds condition. At 6 months, TUG and TUG-DT scores improved by 63.2% (95% CI 32.8–93.6, $p = 0.006$) and 54.0% (95% CI 13.7–94.2, $p = 0.021$) when compared to baseline. In the 20 Meters Walking Test without obstacles, time and the number of steps to complete the task were reduced by 58.0% (95% CI 19.5–125.8, $p = 0.05$) and 65.7% (95% CI 29.7–101.6, $p = 0.009$), respectively. In

addition, stride length was increased by 170% (p = 0.01). Similar results were observed in the 20 Meters Walking Test with obstacles, with time and number of steps improving by 63.3% (95% CI 10.4–116.3, p = 0.03) and 70.1% (95% CI 18.7–121.5, p = 0.021). Findings described above in the 'OFF' meds condition were similar to those observed while patients received medications.

Secondary Outcomes: PDQ39: Six months after SCS, total PDQ 39 improved by 44.7% compared to baseline (from 58.0 ± 20.7 to 32.0 ± 13.3; 95% CI: 29.9–59.5; p = 0.002). Significant improvements were also observed in specific subscores such as Mobility (56.6%; 95% CI: 46.9–66.3; p < 0.001), Activities of Daily Living subscales (28.3%; 95% CI: 8.8–47.8; p = 0.019), Emotional Well-being (53.0%; 95% CI: 16.9–89.0; p = 0.018) and Stigma (78.1%; 95% CI: 50.8–105.3; p = 0.003). Differences between SCS and baseline were not found to be significant for the Cognition (p = 0.39), Social Support (p = 0.39), Communication (p = 0.51) and Bodily Discomfort (p = 1.0) subscores.

UPDRS Motor Scores: At baseline (after an average of 7.8 years from the initial DBS surgery), UPDRS III scores without medication were 33.0 ± 13.7. In the 'ON' DBS, 'OFF' Meds condition improvement following SCS, at 1, 3, and 6 months was in the order of 36.8% (UPDRS III scores 22.0 ± 14.3; p = 0.18; 95% CI: 22.5–96.1), 48.7% (16.2 ± 5.7; p = 0.009; 95% CI 21.9–75.5) and 38.3% (19.7 ± 6.7; p = 0.034; 95% CI: 5.3–64.6), respectively. At 6 months, the UPDRS III score in the 'ON' DBS, 'ON' Meds, 'ON' SCS state (15.0 ± 4.24) was 50% lower than that recorded while patients were receiving DBS and medications prior to SCS (p = 0.018; 95% CI 15.3–86.1; supplementary fig. 1).

Berg Balance Scale: BBS was applied to access static balance and the risk of falls. All patients showed a significant improvement; preoperative scores went from 47.5 ± 4.5 to a post SCS value of 51.5 ± 5.0 (8% increase; p = 0.005).

FOG-Q scores: All patients showed a significant improvement in freezing of gait at 6 months, as revealed by a 56.4% decrease in FOG-Q scores (from 17.8 ± 0.9 at baseline to 7.8 ± 0.9; p < 0.001).

In summary, outcome data suggest that patients treated with SCS had significant improvement in locomotion, PD motor symptoms, freezing of gait, risk of falls and quality of life as compared to baseline.

Blinded evaluations: ANOVA revealed that during the 20 meters walking test, both time (F(2.6)=24.4; p < 0.001) and the number of steps (F(2.6)=22.8; p = 0.002) were different across groups. This was also the case for TUG, with significant differences in time being recorded across groups (F(2.6)=35.5; p < 0.001).

The results described above were largely due to improvements in gait observed during 300 Hz SCS. As compared to the non-stimulation condition, this treatment reduced both time (94.0 ± 70.8 to 30.5 ± 17.3; p = 0.028) and the number of steps (74.0 ± 27.6 to 26.7 ± 17.6; p = 0.03) needed to complete the 20 m waling test, as well as the TUG time (from 36.0 ± 30.1 to 11.8 ± 5.9; p = 0.003). In contrast, SCS 60 Hz was largely ineffective with no significant differences being recorded between this treatment and SCS 'OFF'.

Discussion: In this phase 1 clinical trial we have studied the safety and efficacy of SCS on PIGD in four patients with advanced PD previously treated with STN DBS. To mimic preclinical studies, high frequency stimulation (i.e. 300 Hz) was delivered through paddle electrodes implanted in the upper thoracic spine. Overall, we have objectively recorded a significant and sustained positive clinical response in several gait measurements, including walking and stride length, freezing. Improvement on PIGD occurred within minutes after stimulation onset and was seen in all patients. It lasted for the duration of the study (i.e. 6 months) with no apparent loss of benefit over time. In addition, SCS decreased the number of falls and seemed to synergistically improve UPDRS III scores when administered along with STN-DBS. Following an improvement in locomotion, patients reported a better quality of life, as measured by the PDQ-39.

Because our study had an open label design and patients reported stimulation-induced paresthesias, a concern that needed to be addressed was the possibility of a placebo effect. To specifically address this issue, we performed a blinded experiment in which SCS was randomly delivered at either 60 or 300 Hz. While a similar degree of paresthesias was reported with either setting, gait improvement was only documented when SCS was delivered at 300 Hz.

In 2009, Fuentes et al. showed that thoracic SCS was able to restore locomotion deficits in a rodent model of PD (Fuentes et al., 2009). The authors hypothesized that the effects of high-frequency SCS were primarily due to a disruption in pathological cortico-striatal neuronal oscillatory activity. Similar findings were reproduced by the same group in non-human primates (Fuentes et al., 2009; Santana et al., 2014). In recent work, Santana et al showed that the highly synchronized neuronal activity of cortico-basal ganglia-thalamic structures in a non-human primate model of PD was also blocked by SCS (Santana et al., 2014). Whether this neurophysiological mechanism can also account for the clinical effects in humans remains to be demonstrated.

In preclinical experiments, SCS restored close to normal locomotion patterns right after stimulation was switched on. In the first clinical implementation of this technique, Thevathasan and colleagues failed to show a positive effect of SCS in PD (Thevathasan et al., 2010). Those negative findings raised an interesting discussion about potential mechanism responsible for the sudden relief of akinesia/gait deficits in rodent models (Nicolelis et al., 2010). In addition to the modulation of corticolimbic rhythms, a proposed mechanism was the so-called paradoxical kinesis. This would occur as a consequence of the intense arousal evoked by high frequency stimulation of sensory ascending fibers. Similar to the startle reflex, however, paradoxical kinesis habituates over time and cannot justify a chronic clinical response. In our study, startle-like responses during SCS were avoided by using an SCS system capable of delivering adjustable stimulation, which was finely tuned to induce mild paresthesias. Although some adjustments in stimulation intensity were required over time, we did not observe short-term habituation related to the gait effect produced by SCS. Therefore, it is unlikely that the observed locomotion improvement detected in our study resulted simply from paradoxical kinesis.

After the initial negative findings of Thevathasan et al., a few clinical studies have shown that SCS was able to improve gait and motor symptoms in a total of 24 PD patients. Agari et al. reported a 19% improvement in UPDRS motor scores 3 months after SCS onset in 15 PD patients who also had intractable back and leg pain (Agari and Date, 2012). This was largely due to improvements in gait function and postural instability and associated with changes in bradykinesia or rigidity. As all patients in that trial had moderate to severe pain, however, it was not possible to rule out that the achieved results were a consequence of pain reduction. Hassan et

al. described the effects of bilateral high cervical stimulation in a PD patient with post-traumatic neuropathic pain (Hassan et al., 2013). Remarkably, SCS combined with medications improved UPDRS motor scores by 21% and 42% at 12 and 24 months. In addition, the timed 10 m walk test was also improved by 35% after 24 months. Fénelon et al. reported another patient who underwent routine thoracic quadripolar stimulation for failed back syndrome and subsequently developed PD (Fénelon et al., 2012). After SCS, a 47.6% improvement in UPDRS motor scores was recorded (15.3% add-on effect over medications alone). In contrast to other studies, specific analyses revealed a 40% improvement in bradykinesia, 65% in rigidity, 61.7% in tremor, and 21.5% in walking time after SCS. More recently, Nishioka & Nakajima reported three patients with chronic pain and PD who had significant improvements in both conditions after SCS (Nishioka and Nakajima, 2015).

Overall, our study differs from the ones described above in several ways. First, electrodes were implanted in high thoracic regions and patients received SCS at 300 Hz. In other words, it was the first time the implanted location and SCS protocol matched those employed in animal studies (Fuentes et al., 2009, 2010; Santana et al., 2014). Second, only advanced PD patients who experienced significant PIGD following STN DBS were included. Third, SCS was delivered with a positional system, using a quantitative criterion for defining the stimulation amplitude (105% sensory threshold and presence of paresthesias). This protocol not only led to the positional control of current delivery, but also produced both a much lower level of discomfort following positional changes (Abejon et al., 2014). Finally and most importantly, to clearly ascertain the role of stimulation on gait, we have conducted a blinded experiment comparing the effects of 60 and 300 Hz. Our results show that only the latter frequency was capable of eliciting substantial improvements.

Today, the treatment of PIGD is one of the most challenging problems in Parkinson's disease. This is of importance because PIGD significantly increases the risk of falls (Bloem, Grimbergen, et al., 2001) and collaborates to enhance the morbidity and mortality in advanced PD (Matinolli et al., 2011). Currently investigated neuromodulation treatments for PIGD, particularly in patients who do not improve after STN or GPi DBS, include stimulation of the pedunculopontine nucleus (PPN) or substantia nigra reticulata (SNr). Evidence is now mounting that PPN DBS, particularly when conducted bilaterally, can improve gait and FOG. Such improvement, however, is inconsistent across studies and mostly reported to be mild to moderate (Moro et al., 2010; Thevathasan et al., 2012). While initial studies found that high frequency stimulation of the SNr induced similar improvements in gait and postural instability when compared to STN DBS, (Chastan et al., 2009) recent work suggests that the combination STN/SNr stimulation may yield short-term positive results (Weiss et al., 2011, 2013). In addition to the techniques described above, some degree of improvement may also be reached with rehabilitation therapies (Alves da Rocha et al., 2015) and wearable devices, (Lopez et al., 2014) though this is somewhat limited in patients with advanced PD. With a much less invasive nature SCS may become an attractive alternative to treat PIGD if proven efficacious and capable of producing long-lasting clinical effects.

In summary, our pilot study provides open label evidence that 300 Hz SCS is safe and effective in improving PIGD in advanced PD patients previously treated with STN DBS. Although our findings still need to be corroborated in a larger cohort followed for a longer interval, they do suggest that 300 Hz SCS may elicit significant gait improvements in advanced PD patients.

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#8533

Overlapping of Patient-Specific Models of DBS and Tractography-Based Target Correlated to Motor Improvement in Patients with Parkinson's Disease

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Introduction: Localization of the dorsolateral zone (motor) of the subthalamic nucleus for deep brain stimulation (DBS) in patients with Parkinson's disease (PD) is possible with tractography through the connections from the M1/SMA. However, tractography has not been adequately validated for DBS targeting. In this work, we analyze the overlapping between the patient-specific volume of tissue activated (VTA) and the subthalamic target obtained by tractography correlated with the motor improvement in patients with PD.

Materials and Methods: We include 13 patients underwent bilateral STN-DBS (23 electrodes). We obtained the motor zone of the STN using a method described by our group previously.

Based in the work of Mc Intyre et al., we used the Optivise® software package to obtain the VTA of each clinically effective electrode's contact of every patient. We obtained the UPDRS III score of each side of the patients (23 scores). We computed the percentage of improvement based on the pre and postoperative scores. Finally, we obtained the percentage of overlapping between the VTA and tractographical target of the STN. We used the Spearman correlation to analyze the relationship between the VTA/motor STN and the percentage of motor improvement.

Results: The Wilcoxon test revealed a statistically significant improvement of all patients after STN-DBS ($p = 0.0024$). Correlation analysis showed a positive correlation between the VTA/motor STN and the percentage of motor improvement ($r = 0.58$; moderate correlation) with a statically significant result ($p = 0.048$).

Conclusions: This study suggest that stimulation in the motor part of the STN obtained by tractography is associated with a better motor improvement than stimulation outside of the motor part of the STN.

There is positive correlation between the electrical influence of this tractographical target with the degree of motor improvement.

#8537

DBS for Essential Tremor: Aligning Thalamic and Subthalamic Targets in One Surgical Trajectory

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Keywords: Deep brain stimulation, Essential tremor, Posterior subthalamic area, Ventral intermediate nucleus, Surgical trajectory.

Objective: Evaluating aligning ventral intermediate nucleus (VIM) and posterior subthalamic area (PSA) in one surgical trajectory for deep brain stimulation (DBS) in essential tremor (ET).

Background: Both VIM DBS and more recent PSA DBS have shown to suppress tremor for ET. Considering it is currently not clear which target is optimal for individual patients we wanted to explore both during intraoperative test stimulation. For this, we applied the technique of aligning both targets in one surgical trajectory.

Design/Methods: Technical aspects of planned trajectories, intraoperative test stimulation findings, final lead placement, target used for chronic stimulation and adverse and beneficial effects were evaluated.

Results: In 17 patients representing 33 planned trajectories (16 bilateral, one unilateral), we successfully aligned VIM and PSA targets in one surgical trajectory in 26 (79%) trajectories (15 patients). Average trajectory distance between both targets was 7.5 mm (range 6–10). In 17 aligned trajectories, optimal intraoperative tremor suppression was obtained in PSA. During follow up, optimal active electrode contacts of these leads were in or just above PSA in the large majority of cases. In the remaining 9 aligned trajectories, optimal intraoperative tremor suppression was obtained in VIM (n = 3) or the area just above PSA (n = 6). During follow up, most active electrode contacts of these latter six leads were in VIM. Overall, successful tremor control was achieved in 74% of contralateral body sides, or 69% of patients. Stimulation-induced dysarthria or gait ataxia occurred in, respectively, 56% and 19%. No difference in tremor suppression efficacy or side effect profile was noted between aligned and non-aligned leads, nor between the different anatomical locations of active stimulation.

Conclusion: Alignment of VIM and PSA for DBS in ET is well feasible and enables intraoperative exploration of both in one single trajectory. This facilitates optimal positioning of electrode contacts in these adjacent areas, where multiple optimal points of stimulation can be found. In the majority of aligned leads, both optimal intraoperative tremor suppression and active contacts used for chronic stimulation were in or just above PSA.

#8541

Subthalamic Local Field Potentials Recorded with Bipolar Electrodes as an Alternative to Microrecording

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Keywords: Local field potentials, Bipolar electrodes.

The use of Local Field Potentials (LFP's) to validate deep brain targets such as the subthalamic nucleus (STN) during deep brain stimulation (DBS) surgery is a potentially attractive alternative to microelectrode recording. LFP's are thought to represent subthreshold activity, such as synaptic activity and information flowing to the neurons. LFP's summarize potentials from numerous neural sources and therefore are challenging to interpret. Furthermore, the spatial reach of cortical LFP's may be up to 10 mm, thus it is unclear whether STN LFPs represent locally generated neuronal activity within the STN or volume conductance of the organized neuronal activity generated in the cortex.

In this study we compare three different methods of human STN recordings: monopolar microelectrode spike and LFP recordings, monopolar macroelectrode spike and LFP recordings and differential-bipolar macroelectrode LFP recordings. We performed spatial-spectral analysis of LFPs recorded outside the STN (white matter) and inside the STN (gray matter) during electrophysiological navigation for DBS procedures (150 electrode trajectories in 40 Parkinson's disease patients). Analysis of the correlation between pairs of parallel electrodes (horizontally separated by 2 mm) in different recording configurations was used to estimate the influence of each recording configuration on the origin of the recorded LFPs.

The results of this study suggest that while monopolar micro- and macro-electrode recordings detect LFP's that are largely affected by cortical activity, bipolar macroelectrode recordings can detect more locally generated LFP's. We conclude that differential bipolar macroelectrode LFP recordings of human STN overcome volume conductance effects and reflect neuronal activity generated locally at the STN. We therefore suggest that bipolar macroelectrode LFP recordings might be effectively used in future electrophysiological studies and navigation systems as well as for closed-loop STN stimulation paradigms.

#8544

Changing the Target after Unsatisfactory Outcome of Deep Brain Stimulation in Advanced Parkinson's Disease: Cases from the NSTAPS Trial and Review of Literature

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Keywords: Deep brain stimulation, Subthalamic nucleus, Globus pallidus pars internus.

Objectives: To evaluate the clinical effect of re-operation to another target after failure of initial deep brain stimulation (DBS) for Parkinson's disease (PD).

Methods: We descriptively analyzed the baseline characteristics, the effect of initial surgery and re-operation of NSTAPS (Netherlands SubThalamic and Pallidal Stimulation) patients and previously published cases that underwent re-operation to a different target. The evaluation included motor symptoms at baseline (off-drug and on-drug), after initial DBS surgery (on-stimulation, off-drug), before re-operation (on-stimulation, off-drug), and after re-operation (on-stimulation, off-drug). We evaluated motor symptoms using the Unified Parkinson's Disease Rating Scale motor examination (UPDRS-III). For the NSTAPS, blinded assessments were available at 12 and 36 months after the initial surgery. We dichotomized motor outcome: an off-drug UPDRS-III score improvement of 30% or more one year after DBS compared to baseline is considered a treatment success and less than 30% is considered unsuccessful.

Results: A total of 14 patients were identified in the NSTAPS (n = 8) study and literature review (n = 6).

NSTAPS Trial: The mean off-drug UPDRS-III before the first surgery (baseline) was 45 (range 24–88), and the mean percentage of improvement with levodopa was 71% (range 49–82%). Re-operation occurred between 12 and 67 months after start of DBS therapy. The mean pre-re-operation off-drug UPDRS-III score was 39 (range 22–56) and the mean score after re-operation was 31 (range 18–40), with two postoperative scores missing. In quantitative terms, two of the eight re-operations were considered a success, that is, a UPDRS-III improvement greater than 30%. Subjectively, five of the eight patients considered their re-operation a success.

Literature Review: three articles were identified that describe a total of six cases, of which three patients initially received bilateral GPi DBS and three received STN DBS (supplement 1). The off-drug UPDRS-III score at baseline was not available in most patients and the percentage of improvement on levodopa was available in three patients only (57%, 81%, 74%). Of the patients who were re-operated from STN to GPi none had improvement of their off-drug UPDRS-III scores (–3%, –11%, –22%), but two of them reported subjective improvement. All patients who were re-operated from GPi to STN had a post-operative improvement of the off-drug UPDRS-III (37%, 59%, 64%) and also subjectively experienced improvement.

Summary of all cases: Five out of 11 patients that were re-operated from GPi DBS to STN DBS showed more than 30% improvement of off-drug motor symptoms. Of the three patients re-operated from STN DBS to GPi DBS, none showed more than 30% off-drug motor improvement.

Conclusions: Half the patients re-operated to STN DBS showed objective clinical improvement of more than 30% on the off-drug UPDRS-III score. However, three out of five of these improved cases were from the systematic review, so this finding is prone to a publication bias. None of the three patients re-operated to GPi DBS showed objective improvement. In conclusion, if insufficient clinical improvement is obtained after GPi DBS and patient selection and electrode placement were correct, re-operation to the STN is worth considering. Currently, there are insufficient data that indicate if re-operating from STN to GPi has a comparable effect.

#8559

Subthalamic Deep Brain Stimulation (DBS) Surgery Under General Anaesthesia (GA) and Neurophysiological Guidance While on Dopaminergic Medications: Prospective Comparative Cohort Study

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Keywords: STN, DBS, Dopaminergic treatment.

Objectives: Parkinsonian patients undergoing subthalamic nucleus (STN) DBS surgery have traditionally been required to stop their dopaminergic medications preoperatively. This was done to enable assessment of the effect of intraoperative stimulation on their parkinsonian state. We perform the procedure under GA and prefer to give the patients their medications to avoid a variety of dopamine-withdrawal effects such as pain and stiffness. The authors have previously demonstrated the technical feasibility of STN DBS under GA, with intraoperative microelectrode recording (MER) guidance, in a small cohort of patients who continued on their medications[1]. This paper presents the results of a prospective cohort analysis to verify the outcome of the initial study, and report on wider aspects of clinical outcome and postoperative recovery.

Methods: All patients were allowed to continue their routine dopaminergic medications up until GA was administered. Patients' demographics, duration of PD and L-dopa Equivalent Daily Dose (LEDD) on admission were recorded. The number of intraoperative microelectrode (MER) tracks required to detect satisfactory STN activity, the length of the STN specific MER (LOR), the duration of surgery and the time required for extubation, as well

as the recovery time from GA in the post-anaesthesia care unit in theatres (PACU) were recorded prospectively. Clinical outcome was assessed using Hoen-Yahr scale, the duration of 'OFF' periods during the wake hours, and the percentage of the 'ON' hours where patient had dyskinesia. These variables were prospectively assessed at 6 months postoperatively and compared to the baseline on admission. All perioperative complications were recorded.

Results: 30 consecutive patients underwent the procedure between May 2014-Dec. 2015 while 'on-medications'. This was compared to a similar cohort (26 patients) who underwent the same procedure 'off-medications'. Baseline characteristics (gender, duration of PD, first presenting symptoms, and preoperative LEDD) were statistically comparable between the two groups. Patients in the 'on-medications' group were slightly younger, 60 (51–64) years versus 64 (56–69) years, $p = 0.043$. Results expressed as median (Inter-Quartile Range, IQR).

Both groups were comparable in the number of tracks required intraoperatively to detect satisfactory STN-MER. 60% in the 'on-medications' group and 58% in the 'off-medications' group required only one track on either side of the brain ($p = 1.000$). Analysis of the total LOR for STN- MER (the sum for both sides of the brain) found this to be significantly higher in the 'on-medications' group, with a median of 9 mm vs. 7 mm ($p = 0.037$). A trend towards better recovery from anaesthesia in the 'on-medications' group was noted, with shorter time for discharge from PACU in the 'on-medications' group; 60 (50–84) minutes Vs. 89 (62–120) minutes, $p = 0.09$.

In the 'on-medications' group all clinical outcome measures (Hoen-Yahr, 'OFF' periods, and period of 'ON hours' spent in dyskinesia) have significantly improved postoperatively, $p < 0.001$. Similarly the total LEDD for the 'on medications' group has significantly dropped postoperatively compared to the preoperative baseline, 553 (360–728) mg/day vs. 1221 (1000–1640) mg/day, $P < 0.001$.

No cases of dopamine-withdrawal or problems with immediate postop dyskinesia were recorded in the 'on medications group'. The observed rate of dopamine-withdrawal side effects in the 'off-medications' group was 15%.

Conclusions: The continuation of dopaminergic treatment for patients with PD does not affect the efficacy of the STN- DBS surgery. Neurophysiological markers of intraoperative STN localisation and postoperative clinical outcome measures for this group are comparable to those treated previously with medications withheld. The continuation of routine dopaminergic therapy will reduce the risk of dopamine-withdrawal adverse effects, and appears to be correlated with better recovery in the immediate postoperative period. Continuing medications perioperatively will enhance the patient's experience and should improve clinical outcome.

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#8581

Deep Brain Stimulation in the Caudal Zona Incerta versus Best Medical Treatment in Patients with Parkinson's Disease; A Randomised Blinded Evaluation

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Keywords: Zona incerta, Parkinson's disease, DBS.

Objectives: The aim of the present work was to evaluate in a single blinded randomized manner the effect of bilateral DBS in the caudal zona Incerta (cZi) versus best medical treatment, in a group of patients with PD who would fullfil the criteria for bilateral STN DBS.

Methods: Patients that would normally have been considered for bilateral STN DBS were eligible for participation in this study. Patients were randomized to either bilateral cZi DBS within 1 month or to best medical treatment. The primary endpoints were the differences between baseline and 6 months scores between the two groups for UPDRS III off-medication and PDQ-39. All UPDRS-III evaluations were videotaped with the patients wearing head caps and rated by two assessors unaware of the patients' previous allocation.

Results: Of 20 included patients (10 in each group) one patient randomized to surgery did not accept turning off the DBS and was therefore excluded. Hence, 19 patients were evaluated at 6 months. There were no differences between the groups concerning patients' demographic and clinical characteristics at baseline. Mean UPDRS III scores off-medication on stimulation improved from 33.2 at baseline to 19.4 at 6 months (41.6%, $p = 0.001$). The highest degree of improvement concerned the scores of tremor items of the UPDRS (5.1 off-med at baseline vs. 0.4 on stimulation off medication, $p < 0.002$). There were no changes of scores in the medical group. The on-medication UPDRS III scores did not change in any of the groups.

For PDQ-39, the total index was improved in the surgical group by 8.3 points from 22.8 to 14.5 (36.4%, $p = 0.038$) and in the medical group by 6.1 points from 25.0 to 18.9 (24.4%, $p = 0.028$). While the improvement in PDQ39 was significant within each group, the difference between the groups at 6 months was not significant.

Neither dyskinesia scores nor Levodopa equivalent daily doses did change in any of the groups. Mean stimulation parameters at 6 months were 2.48 ± 0.43 V, 152.2 ± 10.3 Hz and 63.3 ± 9.7 uS. In the surgical group one patient suffered a deep venous thrombosis in one leg three months after surgery. No complications were encountered in the medical group.

Conclusions: DBS in the cZi was in this blinded randomized study demonstrated to be safe and superior to medical therapy alone. The degree of improvement achieved with cZi DBS was somewhat modest compared to the results reported in non-randomized studies of both cZi and STN DBS. The results were, however, broadly similar to the results reported in randomized studies of bilateral STN DBS, with a marked robust effect of cZI DBS on tremor. Further studies are necessary in order to determine the role of cZi DBS and its symptomatic impact profile, in the surgical armamentarium for PD, especially in relation to STN DBS.

#8587

Laser Doppler Flowmetry Guidance during Stereotactic Neurosurgery: A Review of Safety Aspects

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Keywords: Deep brain stimulation (DBS), Intraoperative measurements, Laser doppler flowmetry (LDF), Navigation, Cerbral microcirculation.

The most severe complication in stereotactic deep brain stimulation (DBS) surgery is intracerebral bleeding. Therefor planning of the target site and trajectory is of out most importance. At many clinics intraoperative measurements as microelectrode recording (MER) are common complements to the image based surgical planning. However, MER has a tendence to increase the bleeding incident [1] expecially if several trajectories are chosen. We have developed an optical navigation tool which uses an insertion guide designed with forward looking optical fibres. The guide-probe is designed to fit Leksell® Stereotactic System (Elekta instrument AB, Sweden) i.e. the same dimensions as a radio-frequency lesioning and impedance probe. Connection of the optical fibers to a LDF (Peliflux 5000, Perimed AB, Sweden) can be used to record the cerebral microcirculation and backscattered light reflecting the tissue greyness in front of the guide. The system has been used during more than 120 DBS implantations and typical 'bar-codes' i.e. grey-white matter changes along the insertion path have previously been defined for trajectories towards STN and VIM [2]. Ongoing work focuses on the 'bar-code' for a combined VIM-Zi trajectory.

The aim of the present investigation was to evaluate the LDFs potential as 'vessel alarm', and patient safety during DBS implantations in 50 patients (83 trajectories) at Linköping University Hospital (LiU M182-04, T54-09). Medical record and postoperative radiology were reviewed together with the optical data collected during surgery. All patients were on systemic anticoagulation therapy and undervent a postoperative CT. Recordings were done at 2471 tissue sites. Of these positions 170 (6.9%) spots showed a doubled microvascular blood flow compared to the surrounding. Seventy three (4.3%) of these showed more than five time higher blood flow than the surrounding tissue. High blood flow peaks were most common along VIM trajectories. All trajectories except one were recorded without adverse events. A small heamorrhage was detected with the help of the microvascular blood flow measurements along one preplanned VIM trajectory. In this case both the grey-white matter and blod flow 'bar-codes' deviated from expected shapes. Post-operative evaluation showed that the frame system was dislocated and thus a deviating trajectory recorded [2].

The LDF system is highly sensitive and can detect small microvascular changes and grey-white matter differences on 0.5 mm measurement resolution along trajectories [3]. The LDF measurements can also visualize ventricular and sulci involvement, and thus warn if the blood flow starts to increase in sensitive regions. The microvascular recordings correlates well with the systemic heart frequency and can also display microvascular regulations such as vasomotion and local vessel peaks. With the LDF method's forward looking feature in combination with controlled insertion of the probe, it has a potential to act as a 'vessel alarm' and thus helps further minimizing the risks of bleedings. Future potential applications include vessel tracking in combination with MER and stereotactic optical biopsies for tumour diagnostics.

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#8589

Chronic Directional Deep Brain Stimulation in Movement Disorders – One Year of Clinical Experience

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Keywords: Deep brain stimulation, Directional, Movement disorders.

Objective: Unwanted side effects, induced by current spread into adjacent structures, limit the efficacy of conventional deep brain stimulation (DBS). In Parkinson's disease (PD), the corticospinal tract and the medial lemniscus are correlated with motor and sensory side effects from subthalamic nucleus (STN) stimulation, while the internal capsule is also most often affected in globus pallidus internus (GPi) stimulation. In essential tremor (ET), DBS targeting the Vim/PSA can lead to inadvertent stimulation of the internal capsule and cerebellothalamic fibres, among others, resulting in paresthesia, dysarthria and disequilibrium.

Intraoperative studies in DBS of the STN provide evidence that directional steering of the electrical field can modify thresholds for

both beneficial and side effects. In September 2015, a DBS system for chronic directional stimulation (Boston Scientific) has become available for clinical use.

After one year of experience with directional DBS, we aim to preliminary assess the therapeutic potential of this new technology and explore the surgical and radiologic specifics.

Methods: After classic target planning, DBS leads with a radiopaque marker were implanted employing standard procedures, aiming to implant the three segments of the directional electrodes facing anteriorly, posterolaterally and posteromedially. Intra- and postoperative x-ray and postoperative CCT were conducted to evaluate lead positioning and orientation.

In a pilot study for DBS of the STN, randomized, double-blinded monopolar reviews were conducted and therapeutic vs. side effect thresholds were compared between uni- and omnidirectional stimulation. With the respective optimal settings established, patients entered a two-day double-blinded crossover phase and were then asked to opt for their preferred mode of stimulation. As of now, 10 consecutive patients were included into the ongoing treatment study.

Outside the study, three patients were implanted in Vim/PSA for ET, and one patient with PD had revision in GPi to alleviate early side effects under the use of conventional leads.

Results: Lead Implantation required extra effort only to aim for desired orientation of directional contacts per visual judgment. However, postoperative verification of lead orientation proved difficult, as the orientation of the marker cannot be objectively evaluated on X-ray and conventional CT scans. An algorithm for verification of axial orientation through analysis of CT artefacts is being developed.

During double-blinded clinical testing, unidirectional steering led to increased side effect thresholds in at least one direction compared to omnidirectional stimulation. The blindedly selected favorable direction of stimulation in STN DBS was posteromedial or anterior in most patients. After the blinded two-day crossover phase, the majority of patients opted for the directional stimulation, and all patients so far remain on directional settings for at least one hemisphere.

Conclusions: This study confirms that chronic directional DBS in movement disorders is safe, well tolerated, and may increase the threshold for side effects, thus widening the therapeutic window in comparison to conventional DBS. In an ongoing pilot study for DBS of the STN, most patients opted for directional stimulation after a blinded two-day trial. Larger studies and long-term follow-up are needed to confirm and quantitate the results. As conventional circular stimulation is still feasible with segmented electrodes, it appears safe to explore their use in diverse targets.

#8597

Individualized Parcellation of the Subthalamic Nucleus in Patients with Parkinson's Disease with 7T MRI

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Keywords: Subthalamic nucleus, Ultra-high field MRI, 7 Tesla, Deep brain stimulation, Parkinson's disease, Parcellation, Motor part, Patient-specific.

Background: Deep brain stimulation of the subthalamic nucleus (STN) is a widely performed surgical treatment for patients with Parkinson's disease. The goal of the surgery is to place an electrode in the motor region of the STN while avoiding non-motor regions. However, distinguishing the motor region from the neighboring associative and limbic areas in individual patients using imaging modalities was until recently not possible. Here, we have performed a patient-specific dissection of the subdivisions of the STN using ultra-high field MR imaging to allow for individualized surgical planning.

Methods: We have acquired 7T diffusion-weighted images of seventeen patients with Parkinson's disease scheduled for deep brain stimulation surgery. Using a previously established protocol, the STN's connections to the motor, limbic, and associative cortical areas were used to map the individual subdivisions of the nucleus.

Findings: A reproducible patient-specific parcellation of the STN into a posterolateral motor and gradually overlapping central associative area in all STNs, taking up on average 55·3 % and 55·6 % of the total nucleus volume. The limbic area was found in the anteromedial part of the nucleus.

Interpretation: Our results demonstrate that ultra-high field MR imaging can be used to perform an individualized and highly specific planning of deep brain stimulation surgery of the STN.

#8610

Functional Connectivity of the Subthalamic Nucleus: The Role of Probabilistic Tractography in Deep Brain Stimulation for Parkinson's Disease

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Keywords: DBS, Parkinson's, DTI, Diffusion tensor imaging, tractography.

Introduction: The subthalamic nucleus became the gold standard target for deep brain stimulation in Parkinson's disease in the last 25 years, but the exact mechanism of chronic stimulation is still poorly understood. Some still rely on the hypothesis that only proper placement of DBS leads within the subthalamic nucleus can alleviate most motor symptoms of the disease. As our focus gradually shifts to using segmented, directional leads, understanding anatomical and connectivity relations of the subthalamic nucleus is becoming even more essential.

Methods: 15 patients suffering from Parkinson's disease who underwent deep brain stimulation were enrolled in this study. 3D T1 (1x1x1 mm, isotropic voxels), contrast enhanced T1, T2 (0.5x0.5x1.5 mm), and DTI (32 directions, 2x2x2 mm, isotropic voxels) MRI sequences were acquired preoperatively from each subject on a 3T Siemens Verio scanner. Contrast enhanced CT scans were acquired on the day of the surgery with a Leksell stereotactic frame placed on the patients' head. CT and MRI images were fused to preserve accuracy by creating a semi distortion-free environment. Lead placement has been carried out with the guidance of intraoperative microelectrode recording and macrostimulation. Postoperative contrast enhanced CT scans were acquired at least 6 weeks after surgery to exclude pneumocephalus or brain shift during analysis. Postoperative CT scans and T2 sequences were registered to anatomical T1 reference images using Flirt (FSL 5.0.9, FMRIB, Oxford). Preprocessing of DTI images has been carried out using FSL. Cortical parcellation was done using Freesurfer (ver. 5.3., Martinos Center for Biomedical Imaging, Harvard University). Cortical regions were manually checked for artifacts or inconsistencies, the subthalamic nuclei has been delineated manually by too independent experts. Probabilistic segmentation of the subthalamic nucleus was carried out using FSL probtrackX, using default settings and modified Euler streaming. Postoperative outcome was measured using UPDRS III motor scale by an independent neurologist, at least one year after surgery.

Results: Results of probabilistic tractography showed statistically significant distinct functional subgroups within the subthalamic nucleus, connecting to limbic, dorsolateral prefrontal, presupplementer motor, supplementer motor, and motor regions respectively. Clinical outcome was measured at least one year after surgery by selecting the best stimulation contacts, chosen by a neurologist independently based on clinical signs only. Best clinical outcome could be achieved by using contacts closest to pathways traversing and terminating at portion of the subthalamic nucleus connecting to the supplementer motor area. Average outcome in the whole population was 8,92/108 on the UPDRS III scale.

Conclusion: Probabilistic tractography is able to reveal functional subgroups within the subthalamic nucleus. Estimating fiber distribution within and surrounding the nucleus can provide even more sophisticated targets, while also contributing to programming conventional and directional leads.

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#8611

Meta-Analysis of 94 Studies Assessing Adverse Events Associated with Deep Brain Stimulation Surgery and Implanted Hardware

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Keywords: Adverse event, Complication, Infection, Erosion, Revision, Hemorrhage.

Background and Objective: Adverse events (AEs) related to surgery or implanted devices are feared the most by patients to be treated with deep brain stimulation (DBS) and such AEs have a detrimental impact on clinical outcome and quality of life.

Methods: The 'PubMed' database was searched using the following search term: ((deep brain stimulation[Title]) AND ((complication*[Title]) OR (adverse event*[Title]) OR (hemorrh*[Title]) OR (infect*[Title]) OR (explant*[Title]))). In addition, relevant studies assessing AEs, in particular prospective and monitored trials for Parkinson's disease, tremor, or dystonia, were included. The following three categories were used to assess AEs: (1) hemorrhage and other intracranial complications, such as brain infarction or brain abscess; (2) infections or erosions resulting in complete or partial hardware removal as this resulted in interruption of DBS therapy; (3) lead revisions due to fracture, misplacement, migration, or loss of effect since this involves an additional intracranial procedure. All three categories can be accurately assessed even in a retrospective manner provided that postoperative imaging is performed and that a complete set of surgical reports is available for all patients. The number of AEs was related to the number of patients but not the number of procedures

or the number of electrodes implanted as this generates the most informative rates and does not result in the dilution of AEs rates. Additional analysis based on patient-years (mean follow-up x patients) served to account for long-term complications and to put studies with different follow-ups on a common denominator. AE rates were calculated (i) among studies ('non-pooled' analysis) and (ii) also determined by summing up respective AEs of all applicable studies and by dividing this number by the total number of patients included in these studies ('pooled' analysis).

Results: Although, all three categories represented complications that had to be rated as serious AE and at least severe AE in many instances exact numbers could not be derived, even in high-ranked thoroughly monitored trials. The average rate of intracranial complications was 3.8% and 3.4% for non-pooled and pooled analysis, respectively. It did not differ between 9 studies involving >300 patients and 31 studies involving <100 patients (3.8% each; non-pooled). However, 'pooled' analysis of complications rates revealed that the incidence of intrcranial complications was lower in larger studies (3.2 vs. 3.7% for studies having included >300 vs. <100 patients, respectively). Interestingly, in monitored trials the reported rate of intracranial complications was the lowest (3.0%). This may be due to the fact that the inclusion criteria of those studies exclude patients exhibiting a higher risk for hemorrhages and centers may tend to suggest study participation rather to healthier patients. The rate of infections that required hardware removal (4.3% and 3.8%, pooled and non-pooled, respectively) or lead revisions (5.8% and 4.4%) was markedly lower in larger studies with >1000 patient-years of cumulative follow-up (3.9 and 3.4% for infections and 5.8 and 4.4% for lead revision) compared to smaller studies with <100 patients and/or <250 patient-years of follow-up (4.7 and 5.0% for infections and 7.7 and 8.3% for lead revision). These data were in agreement with a lower incidence of infections and lead revisions per patient-years. The rates for infections and lead revisions were always lower with 'pooled' analysis as opposed to 'non-pooled' analysis. This also indicates that infection and lead revision rates differed depending on study size with higher rates in series with fewer patients and shorter follow-up. Notably, the risk of infection with complete or partial hardware removal was comparably high in monitored trials (>5% for all assessments).

Conclusions: We propose three categories for the assessment of DBS surgery and hardware-related AEs for the following advantages: unequivocal definition of AEs; coverage of the most relevant complications from a patient's perspective; possibility of accurate retrospective assessment; suited for the assessment of different studies as performed in this meta-analysis. All hardware-related complications should also be expressed in patient-years serving as the best common denominator for in-between study comparison. With the proposed approach valid data can be gathered at any time and such data are suited for proper patient counseling by treating centers.

#8627

A Stepwise Algorithm for Tractography-Based Targeting in Movement Disorder Surgery

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Introduction: Diffusion tensor imaging can be useful to delineate the structural connectivity of surgical targets for deep brain stimulation in brain. However the concerns surrounding imaging artifacts and preprocessing steps make it challenging to translate imaging findings into surgical targeting. We report the role of diffusion imaging algorithms for the purposes of targeting ventral intermediate (VIM) nucleus for tremor surgery, and corroboration of accuracy by comparison of location of tracts during intraoperative microelectrode recordings.

Methods: Diffusion (60 gradient directions) and structural imaging in 3Tesla MR was used in a cohort of 6 patients (3 essential tremor, and 3 with tremor dominant Parkinson's disease). Raw diffusion data was preprocessed offline with eddy-current and registration-based distortion corrections. After conversion to DICOM, the images were uploaded into the StealthViz workstation (Medtronic Inc., Minneapolis, MN). The diffusion data was rigidly aligned with the high resolution 3D T1 sequence, to allow for anatomical/diffusion mixed images. This also permitted determination of accuracy of coregistration by comparing the location of 10 different anatomical landmarks in the proximity to the thalamus (anterior commissure, posterior commissure, bilateral superior colliculi, bilateral body of fornix, bilateral superior cerebellar peduncle, and the posterior and inferior borders of the splenium of the corpus callosum in the midsagittal plane). The registration was considered adequate if the 7 out of these 10 landmarks were within ≤2 mm between the T1 and diffusion-weighted images. After this stage deterministic FACT-based tractography was performed. Prior to ROI placement, the tensor calculation results were verified by looking at the direction of the principal eigenvector in selected location (color FA map). The pyramidal tract and medial lemniscus were tracked using standard tracking parameters (seed density = 1, FA stop value 0.2 and tracking angle 45-600. VIM tractography was only performed if all the previous preprocessing steps were satisfactorily completed. The location of the tracts were then retrospectively correlated to the microelectrode intraoperative recordings.

Results: We were able to successfully determine the location of VIM by visualizing the dentatorubrothalamic tract (DRT) in all the patients. The mean error in anatomical alignment between scans was less than 2 mm in 7 of the chosen landmarks for this cohort. We observed consistent discrepancy in the alignment of the anterior commissure, likely originating from the susceptibility effect from air-filled sphenoid sinuses despite being minimized by our pre-processing steps. During MER, the areas with intraopera-

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tive stimulation-induced tremor suppression were consistently overlapping with the DRT projection in each patient. The entire preprocessing process take 80 minutes per subject.

Conclusions: We present here a framework to perform tractography based targeting and include the necessary steps to maximize accuracy. Use of this methodology also permits improved visualization of white matter tracts from small ROI for targeting purposes. Key steps in the use of tractography based targeting include the ability of mixing diffusion and anatomical images, assessment of coregistration accuracy and visualization of DRT.

#8665

Image Guided and Verified Subthalamic Stimulation (STN-DBS) for Parkinson's Disease Performed Under General Anesthesia Is Providing the Same Therapeutic Window as a Local Anesthesia STN-DBS Procedure

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Keywords: STN – DBS – Parkinson – General anesthesia – Image guided stereotaxy.

Background: The best surgical procedure for subthalamic nucleus (STN) deep brain stimulation (DBS) implantation remains a subject of debate.

Objectives: To study the impact of the absence of awake clinical evaluation during STN-DBS image guided and verified on parameters of stimulation and clinical outcome for Parkinson's disease (PD) patients.

Methods: 13 PD patients who underwent bilateral STN-DBS image guided and verified under general anaesthesia (GA) with a minimal intraoperative evaluation (side effects only), were compared to 10 patients operated under local anaesthesia (LA) with a complete testing. The primary endpoint was the therapeutic window between the mean threshold of intensity for motor improvement and the mean threshold of intensity for stimulation side effects, on the active contacts at 1 year post-operative, expressed in volts (V). Motor scores were also measured.

Results: The mean therapeutic window on the right STN was 2.06 V in the LA group and 2.4 V in the GA group ($p = 0.316$). For the left STN, it was 2.06 V in the LA group vs. 2.16 V in the GA group ($p = 0.811$). The Unified PD rating scale III score in the 'off drug-on stim' condition improved at short term in both groups (40.3% in the LA group and 49% in the GA group), with no significant difference between the 2 groups ($p = 0.336$). UPDRS III ' on stim – on drug' improved from 70.7% in the GA group and 57% in the G group ($p = 0.36$).

Conclusion: Asleep, image-guided and verified STN-DBS provide the same motor results as awake surgery and at the same time maintain the therapeutic window, if pre and intraoperative imaging and surgical techniques enable an accurate STN identification and positioning of the DBS lead.

#8744

Neuropsychological Outcome in Subthalamic Nucleus Stimulation Surgeries with Electrodes Passing through the Caudate Nucleus

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Keywords: STN-DBS, Caudate, Neuropsychology.

Background: Deep Brain Stimulation (DBS) of the Subthalamic Nucleus (STN) in Parkinson's Disease (PD) is associated with postoperative cognitive decline. One of the proposed underlying mechanisms is the surgical procedure with the lead trajectory penetrating the caudate nucleus.

Objective: To study whether penetration of the caudate nucleus affects neuropsychological outcome.

Methods: Neuropsychological and imaging data of 30 PD patients who underwent bilateral STN-DBS were analysed. Lead trajectories were evaluated leading to one group with ($n = 10$) and one group without penetration of the caudate nucleus ($n = 20$). The neuropsychological performance of each group was compared to baseline, both at three and twelve months postoperatively.

Results: Only Trail Making Test part B (TMT-B) showed an interaction effect within the groups over time at three months postoperatively. At twelve months postoperatively, there was only a main effect of time with a decrease of performance in TMT-B for both groups. Also verbal fluency showed a significant decrease over time for both groups at three and twelve months postoperatively.

Conclusion: Caudate nucleus penetration affects cognitive flexibility only at short term after surgery.

#8761

Intraoperative Neurophysiological Markers of the Success of STN-DBS: Microelectrode Recordings, Stimulation, Local Field Potentials?

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Keywords: LFP MER Parkinson.

Introduction: Deep brain stimulation (DBS) of the subthalamic nucleus (STN) is advocated in patients with advanced Parkinson's disease (PD). Microelectrode recording (MER) is one of the intraoperative targeting modalities performed in conjunction with stimulation. In addition, the occurrence of β oscillations of the local field potentials (LFP) has been suggested as another targeting modality. The goal of this observational study was to evaluate which intraoperative neurophysiological markers are most predictive of the STN-DBS efficacy.

Methods: Thirty-nine consecutive patients with PD and with a follow up of to at least one year post surgery were included. The efficacy of STN-DBS was evaluated using the MDS-UPDRS part III (score OFF antiparkinsonian medication and ON DBS at one year, versus preoperative OFF antiparkisonian medication).

MER were recorded and intraoperative stimulation thresholds were determined for the therapeutic effects on rigidity and for the internal capsule stimulation (Neurostar, GE; 130 Hz, 60 μs). LFP were recorded from the macrocontact of the microelectrodes (FHC, USA) at the time it was positioned for stimulation (MR plus, GE). β power, computed from LFP [11–31 Hz], recorded at the site chosen for stimulation were compared to that recorded above the STN. Coefficients of determination (R^2) were computed to analyze which proportion of the variance of the STN-DBS efficacy could be explained by these neurophysiological markers.

Results: None significant linear regression was found between the STN-DBS efficacy and the stimulation thresholds of either the effects on rigidity, the magnitude of rigidity improvement, the threshold of internal capsule stimulation or the stimulation range ($R^2 = 0.03$, $p = 0.34$; $R^2 = 0.09$; $R^2 = 0.09$, $p = 0.07$; $R^2 = 0.07$; $p = 0.16$; respectively). Again none significant linear correlation was found between the STN-DBS efficacy and the lenght over which STN cells were recorded ($R^2 = 0.03$, $p = 0.33$).

On the contrary, linear regression was significant between the change in β power and the STN-DBS efficacy ($R^2 = 0.35$, $p < 0.05$). To better analyze the role of b oscillations, additional sigmoidal regression was performed between the change in β power and the STN-DBS efficacy ($R^2 = 0.75$).

Discussion and Conclusion: Here intraoperative stimulation thresholds had no determinant predictive value of the STN-DBS success. New directional electrodes, allowing adaptation of the electrical field dedicated to avoid stimulation of the internal capsule, should reduce again the role of intraoperative stimulation. Changes in β power accounted for 75% of the variance of the STN-DBS efficacy, confirming the major interest of this intraoperative neurophysiological marker, which could contribute to simplify intraoperative procedure and improve patients comfort.

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#8795

Neuronal Firing Activity in the Basal Ganglia after Striatal Transplantation of Dopamine Neurons in Hemiparkinsonian Rats

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Keywords: Globus pallidus, Entopeduncular nucleus, Oscillatory activity.

Objective: In Parkinson's disease (PD) patients and in 6-hydroxy-dopamine (6-OHDA) lesioned rats, the loss of dopaminergic (DA) neurons in the substantia nigra pars compacta and the resulting DA depletion in the striatum lead to altered neuronal activity and enhanced beta activity in regions of the direct and indirect pathway of basal ganglia. Intrastriatal graft implantation of DA neurons has been shown to re-innervate the host brain and restore DA input.

Methods: Female Sprague Dawley rats with 6-OHDA lesions were transplanted with cells derived from the mesencephalon of E12 rat embryos in the striatum. 6-OHDA lesioned and naïve rats served as controls. Thereafter, the effect of intrastriatal grafts on neuronal activity of the globus pallidus internus (GPi), the output nucleus of the basal ganglia, and the globus pallidus externus (GPe), a key region of the indirect pathway, was tested.

Results: The rotational behavior induced by injection of DA agonists was alleviated after intrastriatal graft implantation. Electrophysiological extracellular recordings revealed enhanced firing rate in the entopeduncular nucleus (EPN, the equivalent to the GPi) and enhanced measures of irregularity in the globus pallidus (GP, the equivalent to the GPe). Analysis of firing patterns in 6-OHDA lesioned rats revealed reduced regular firing in both regions, which was accompanied by enhanced burst and irregular firing in the EPN and enhanced irregular firing in the GP. In both regions, intrastriatal DA grafts normalized altered firing activity. Analysis of oscillatory activity revealed enhanced beta activity in both regions, which were reduced by intrastriatal DA grafts.

Discussion: In summary, DA grafts compensate functional deficits and neuronal activity of the basal ganglia indirect and direct pathway.

#8803

Microvascular Decompression for HELPS Syndrome: A Novel Cranial Neuropathy

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Keywords: Microvascular decompression, HELPS syndrome, Laryngospasm.

Introduction: We describe a novel cranial neuropathy, hemi-laryngopharyngeal spasm (HELPS syndrome), successfully treated with microvascular decompression (MVD) in n = 3 patients. These patients presented with a common history of intermittent throat contractions, some escalating to life-threatening respiratory distress. We postulate that this previously unrecognized medical condition is due to a vascular compression of the upper rootlets of the vagus nerve.

Methods: The clinical presentation, pre-operative investigations, intra-operative findings and long term follow-up of three HELPS syndrome patients are presented.

Results: All three patients presented with intermittent but progressively severe throat contractions described as 'choking'. This led to emergency intubation in Patient 1 on two occasions and tracheostomy in Patient 2. Botulinum toxin injections in the throat reduced the severity of the spasms but did not stop them. Additional symptoms included a sensation of tongue enlargement (Patient 1) and intermittent cough triggered by a 'tickling sensation' in the carina (Patient 3). Examples of pre-operative video laryngoscopy will be presented. Pre-operative MRI suggested a vascular compression of the vagus nerve. MRI sequences, optimized to reveal this anatomy, will be presented to highlight the pre-operative diagnosis. All patients underwent MVD and the intraoperative imaging will be presented. One-year follow-up is available for Patient 1 (no further spasms) and short term follow-up is presented for Patients 2 and 3.

Discussion: This syndrome may have been previously described in the otolaryngology literature as 'episodic laryngospasm' – a condition felt to be due to a psychiatric disorder or acid reflux. Prior to her neurosurgical referral, our Patient 1 was encouraged to seek psychiatric help for her condition. We propose that the condition caused by a vascular compression of the special visceral efferents of the vagus nerve (upper rootlets) with resulting pressure atrophy of the insulating myelin sheaths. In common with hemifacial spasm, HELPS syndrome has a unilateral etiology, causes intermittent but progressive muscle spasms which can occur while sleeping. We postulate that the additional symptoms such as a sensation of tongue swelling and cough may be due irritation of vagal general visceral afferent fibres.

Conclusion: We describe a novel cranial neuropathy with pre-operative imaging, video laryngoscopy, intraoperative imaging, and long-term follow-up. Similar to other neurovascular compression syndromes (trigeminal neuralgia, hemifacial spasm, glossopharyngeal neuralgia), HELPS can be successfully treated with MVD. Misdiagnosis as a psychiatric or allergic condition will predictably lead to unsuccessful treatment while over-diagnosis will lead to unnecessary neurosurgery. With wider recognition of this syndrome, additional features may come to light. It is interesting to postulate what symptoms may be triggered by irritation of the general visceral efferents. We encourage neurosurgeons to partner with laryngologists in treating HELPS syndrome.

#8825

Gammaknife Thalamotomy for Tremor: Neuro-Imaging Response Variability at One Year Follow-Up in a Cohort of 169 Consecutive Patients

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Keywords: Gammaknife, Thalamotomy, Neuroimaging.

Objective: This study aims at reporting the variability of the individual response to GK thalamotomy for the treatment of intractable tremor through the analysis of postoperative MR neuro-imaging features of the thalamic lesion and at establishing correlations with the clinical results.

Methods: Between April 2004 and March 2015, a Vim Gammaknife thalamotomy was performed in 319 patients for essential or Parkinsonian tremor in Marseille University hospital with a very stereotyped procedure. A neuro-imaging and clinical assessment was performed at one year FU for 253 patients. The volume of the lesion defined as the whole area of post-contrast enhancement was calculated for each patient in mm^3 and the amount of edema evaluated according to a semi-quantitative scale. The coordinates of the centre of the lesion in relation to the coordinates of the planned target and also regarding AC-PC landmarks were analyzed. A comprehensive clinical evaluation by expert neurologists was performed at the same time. Statistical analysis was performed using R software (R Studio Version 0.98.1091).

Results: Clinical and imaging data were analyzable and reviewed for a total of 169 patients. The median volume of the lesion at 12 months FU (±3 months) was 89.5 mm^3 (Mean = 175, Min:0, Max: 1890, SD: 284). Lesion volume was found to be 4 times above mean in 10 *'hyper-responder'* patients (764–1890 mm^3; 6.1% of patients) and 4 times below in 36 *'hypo-responders'* (0–44 mm^3; 22%). The amount of edema around the lesion, according to our semi-quantitative scale was found to fit into a Gaussian distribution. The discrepancy between the coordinates of the planned target and the centre of the lesion visible upon FU was minimal (in terms of mean (median, min, max, SD) respectively: $\Delta x = 0.47$ (0.4; 0–2.6; 0.43), $\Delta y = 0.45$ (0.3; 0–3.5; 0.45) $\Delta z = 0.65$ (0.6; 0–2.3; 0.21), mainly ascribable to the fusion process of the FU im-

ages and did not account for clinical failure. In this cohort, the center of the lesion on imaging was located 14.7 mm laterally to the midline (14.81;10.3–18.4), 7.4 mm anterior to PC (7.32; 3.1–9.9) or 5.0 mm (median value) posterior to mid-commissural point. A correlation was established between the volume of the lesion and the percentage of tremor reduction at one year follow-up (Pearson's coefficient of correlation $r = +0.22$, $p = 0.018$). Chronoradiobiological parameters such as time at the outset of treatment were not found to explain the hypo or hyperresponsive patterns. Beam-on time was not correlated to the type of response either.

Conclusions: As previously shown in a much smaller series of patients, the patients with respect to the volume of the lesion and amount of surrounding oedema fall into three response profile types (normo, hypo and hyper-responders) that correlate with the clinical outcome. These data confirm our previous results derived from 50 patients with blinded analysis of clinical outcome (Witjas and al. Neurology, 2015). Factors involved in the variability of the response to GK thalamotomy are of utmost importance and currently under investigation.

#8897

Somatotopic Organization of the GPi in Dystonic Patients

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Keywords: Dystonia, DBS, Somatotopia.

Dystonias are characterized by a wide range of involuntary movements and postures, which can be focal or generalized. It seems clear that the basal ganglia play a central role in these symptoms, although the pathophysiological mechanism remains unclear. Although the nuclei of the basal ganglia are functionally segmented and have a somatotopic organization, it is unclear how different dystonic phenotypes relate to alterations of firing patterns in these networks.

We performed single-unit intraoperative MER in 34 patients undergoing GPi DBS for different types of dystonias under general anesthesia (18 myoclonus dystonia, 13 generalized, 3 cervical). Epidemiological characteristics were recorded with the preoperative Burke-Fahn-Marsden dystonia rating scale (BFMDRS). MER of the GPi and GPe were analyzed offline with features of these recordings such as mean firing rate, interspike interval, coefficient of variation. We also determined burst and pause patterns as well as oscillatory activity. MER localizations were determined using our in-house anatomo histological 3D atlas. We compared clinical characteristics, such as the type of dystonia, its localization and side predominance with electrophysiological and anatomical data.

We collected 770 single unit recordings from 34 patients of Gpi & Gpe neurons with a mean recording time of 44.3s, a signal to noise ratio of 2.6 ± 1.4. The mean rate was 23.7 Hz.

There was a correlation between the severity of symptoms and the burst and pause patterns. Furthermore, focal dystonia electrophysiology differed from that of generalized dystonia.

Oncology

#8453

Stereotactic Destruction of Deep Cerebral Gliomas: A Cryosurgery Method

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Keywords: Neurosurgery, Cerebral tumors, Stereotaxis, Cryosurgery, MRI, PET.

According to some data, about 30% of patients with cerebral gliomas are considered to be inoperable due to the location of neoplasms in deep-seated and eloquent areas of the brain. However, it is well known that the effectiveness of treatments such patients strongly depends on possibility end extent of tumor resection, and patients treated only with the chemotherapy and irradiation demonstrate decreased survival rates as compared to operable cases. Radiosurgery is not always suitable in such situations. This problem can be dissolved due to the stereotactic method of neurosurgery operations which allows making operations in the deep areas of a brain thanks to a minimum invasive surgical approach and precision preoperative planning.

Last years, the method of stereotactic destruction of deep brain tumor by means of laser heating began to enter in neurosurgical practice. In this method, the ablation of tumor with a laser is performed under MRI control (Jethva P.R. et al., 2012; Sloan A.E., 2013). There are also reports about stereotactic radiofrequency termoablation of brain tumors (Chrastina J. et al., 2008; Takahashi H. et al., 2009). Because of this, patients with difficult-to-access brain tumors can be cured with a relatively low risk of complications.

But in our opinion based on the literature in the field of general and neurologic oncology and also on our own experience, a cryosurgery stereotactic ablation of brain tumors has some advantages. Among of them there are predictability of shapes and dimensions of tumor cryonecrosis foci formed by a cryoprobe; a rather mild response of adjacent tissues; possibility of an exploratory (reversible) impact on tissue within the temperature range of $-20\,^{O}C$–$30\,^{O}C$; and also ablastic, hemostatic and immunostimulating effects.

We have designed the special cryosurgical device for the purposes of stereotactic neurosurgery. It cools the brain tissue in a target zone up to $-73\,^{O}C$ resulting to a formation of a zone of cryonecrosis within a tumor. This device uses a solid carbon dioxide (dry ice) as a cooling agent, and has some advantages over devices, using liquid nitrogen. They include easy control of temperature at an active tip of a cryoprobe, its good adhesion to a brain tissue, absence of 'icy fractures' of a frozen tissue, simplicity and safety.

In patients with deep-seated gliomas, we perform a multi-positional destruction of neoplasms using the cryosurgery device and stereotactic apparatus. Stereotactic targeting is based on results of preoperative MRI fused with ^{11}C-methionine PET/CT of brain.

The maximum accumulation of ^{11}C-methionine indicate the most malignant zones of tumors to be selectively biopsied and then stereotactically ablated. During operations, we insert a cryoprobe into intratumoral target points through a burr hole by means of stereotactic manipulator and perform consecutive cryoexpositions. Operations are made under local anesthesia for possibility of performing the neurological control on patient, considering the deep and eloquent location of tumors. Before the freezing, we perform the reversible (diagnostic) cooling of target points to the temperature of –20–30^{O}C to prevent the possible side effects. A monitoring of operation is also provided with a neuronavigate station and intraoperative ultrasound scanning.

From 2000 by now we have operated 158 patients with tumors located in thalamus, cerebral peduncle, insula, corpus callosum, basal ganglia, deep-seated areas of temporal, frontal and occipital lobes, central gyri. There were two groups of patients. In the first group, deep seated tumors were less than 3 cm in diameter. These tumors were destructed totally during stereotactic surgery. In the second group, with larger lesions, we selectively ablated only the areas of the maximum ^{11}C-methionine accumulation regarded as zones of maximum cells proliferation. Postoperative mortality was about 1%. The majority of cases had no worsening of life quality: permanent impairment of a neurologic state was watched only in 8.5% of patients. The survival rate in the operated cases was reliably higher than in patients treated with radio- or chemotherapy in every group of patients with grades II, III and IV tumors. Moreover, it was almost identical as in patients underwent total removal of tumors. Thus MRI/PET-guided stereotactic cryodestruction is effective and relatively safe method for treatment of patients with brain tumor localization prohibiting their conventional removal.

#8535

Extended Glioma Resection by Prehabilitation Induced Plasticity

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Introduction: The more extensive resection of brain gliomas, the greatest the impact in survival of these patients. The aim of this study is to find out if pre-surgical cortical electrical stimulation of the tumoral eloquent areas, coupled with intensive neurological prehabilitation, would accelerate plasticity and thus, a more extensive resection.

Methods: We report on five patients with gliomas involving eloquent brain areas identified by intraoperative stimulation mapping. A grid of electrodes was placed over the residual tumor, and continuous cortical electrical stimulation was targeted to the tumoral eloquent areas. The stimulation intensity was adjusted daily to provoke a mild functional impairment while the function was intensively practiced.

Results: The required stimulation intensity to impair function increased progressively in all patients, and all underwent another operation 33.6 days (mean; range: 27–37) later, when the maximal stimulation voltage in all active contacts induced no functional deficit. In all cases, a substantially more extensive resection of the tumor was possible. Intraoperative mapping and functional magnetic resonance imaging demonstrated a plastic reorganization, and all previously demonstrated eloquent areas within the tumor were silent, while there was new functional activation of brain areas in nearby regions or towards the contralateral hemisphere.

Conclusions: Cortical electrical stimulation and appropriate neurological prehabilitation prior to surgery in patients with WHO grade 2 and 3 gliomas affecting eloquent areas can help maximize tumor resection and, thus, improve survival while maintaining function.

Pain

#8409

Peripheral Nerve Stimulation of Brachial Plexus Nerve Root and Suprascapular Nerve for Chronic Refractory Neuropathic Pain of the Upper Limb Pain

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Keywords: Peripheral nerve stimulation, Upper limb pain, Brachial plexus, Suprascapular.

Few options exit to treat medically refractory upper limb neuropathic pain. Chronically implanted peripheral nerve stimulation (PNS) may be a solution in cases of topographically limited pain due to a peripheral nerve lesion, when spinal cord stimulation is not possible or inefficient.

We report the outcome of a consecutive series of 26 patients suffering from chronic refractory upper limb neuropathic pain treated by brachial plexus nerve root stimulation o or suprascapular nerve stimulation. The technique consisted in the percutaneous, ultrasound-guided, implantation of one electrode (Pisces Quad, Medtronic) close to the suprascapular nerve or the cervical nerve roots within the brachial plexus. All the patients underwent a trial stimulation using externalized lead during 10–15 days. In case of positive trial, the electrode was then connected to a subcutaneous stimulator (Itrel 3 or 4, Medtronic). Chronic stimulation parameters were: mean pulse width 168 microseconds (range 90–210), mean frequency 56 Hz (range 20–85), mean voltage 1.13 Volt (range 0.3–2.1 V). The stimulation voltage was set below the threshold inducing muscle contractions or paresthesia.

In this study, 24 patients could be evaluated and 2 patients were lost immediately after surgery. After one year of stimulation, 65% of the patients were improved ≥50%, including 12 patients (46%) improved ≥70%. At last follow-up (mean follow-up 28 months), the mean pain relief was 68%. Out of 20 patients still using the

stimulation, 12 were very satisfied, 6 were satisfied, and 2 were poorly satisfied. Four patients were explanted due to loss of efficacy or complications. Medications related to chronic pain were completely stopped in 6 out of 20 patients after the surgery, reduced in 9 and unchanged in 5. Complications were: shock-like sensations (2 cases), superficial infection (1), electrode fracture (2) and electrode migration (2).

In this pilot study, suprascapular nerve or brachial plexus roots PNS provided a relatively safe, durable and effective option to control upper limb neuropathic pain.

#8504

Gamma Knife Radiosurgery for Glossopharyngeal Neuralgia: A Bicentric Experience of 21 Patients

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Keywords: Radiosurgery, Pain, Neuralgia.

Objective: Glossopharyngeal neuralgia (GPN) is a very rare pathology (0.7–0.8/100.000). Patients usually describe short episodes of paroxysmal pain, beginning at the base of the tongue and pharynx and irradiating towards the neck and the internal ear. We aim at reviewing our bicentric experience (Marseille and Lausanne University Hospital) in patients treated with Gamma Knife surgery (GKS) for idiopathic GPN.

Methods: Between 2003 and 2015, 21 patients were treated with 25 procedures. Eleven were women and 10 were men. All cases fulfilled the pharmaco-resistance criteria. Were analyzed patients with at least 6 months follow-up. GKS using a Gamma Knife (model B or C or Perfexion) was performed, based on both MRI and computer tomography targeting. A single 4-mm isocenter was positioned in the cisternal portion of the glossopharyngeal nerve at a mean distance of 14.6 ± 3 mm (range 9.3–23.5) anteriorly to the emergence of the nerve. The target was placed in the cisternal part for 2 and close to the glossopharyngeal meatus in 23 procedures. The mean maximal dose was 81.4 ± 6.7 Gy (range 60–90). Three cases have had previous microvascular decompression (MVD), which was effective for 2, 8 and 13 years, respectively.

Results: The mean follow-up period was 5.2 ± 3 years (range 0.9–12.1). At 3 months follow-up, 91.6% of the cases were pain free (BNI classes I to IIIA). At one year, 81.8% were still pain free (BNI classes I to IIIA), with 60% of them being BNI class IA. Recurrence appeared in 59.1%, in a mean time of 13.6 ± 10.4 months (range 3.1–36.6). Of them, 35% were controlled with medication and 25% (3 cases, 4 procedures) underwent a new radiosurgical procedure after 7, 17, 19 and 30 months, respectivelly. From these cases, two needed another open surgical procedure, with one undergoing a termocoagulation and another a neurotomy. At last follow-up, 16 cases (80%) were still pain free (BNI I-IIIA, 60% BNI IA). No complication was reported.

Conclusion: As in all cranial neuralgias, the reference technique remains MVD, as it addresses the cause (e.g. the neurovascular conflict). Radiosurgery is a valuable alternative, less invasive, with a very high rate of efficacy, in the absence of complications. The most important aspect is that the fifth nerve is easily identifiable, while the ninth nerve remains more challenging, so as its targeting. A multidisciplinary approach including a neurologist and neuroradiologist might be necessary, both for diagnosis and imaging purposes.

#8545

Medial Gamma-Thalamotomy for Intractable Pain

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Keywords: Gamma knife, Medial thalamotomy, Intractable pain.

Objective: Ablative procedures are still useful in the treatment of intractable pain despite the proliferation of neuromodulation techniques. Here we present the results of gamma knife thalamotomy (GT) in various pain syndromes.

Methods and Patients: Between 1996 and 2015, we performed unilateral GT in 18 patients (F:M = 12:6; age range 53–89, mean 80 yrs) suffering from various severe pain syndromes (3 thalamic pain, 5 postherpetic trigeminal neuralgia [TN], 4 resistant classic TN, 3 secondary TN, 2 TN with multiple sclerosis, 1 phantom pain), in whom conservative treatment had failed. The median follow up was 22 months (range 12–78 months). Invasive procedures for pain release preceded in 13 patients: gamma knife irradiation of the trigeminal nerve, balloon compression or glycerolysis in the cavum Meckeli. The Leksell Sterotactic Frame, Gamma-Plan Software (Elekta) and T1- and T2-weighted sequences acquired at 1.5 T (Siemens Avanto) were used for localization of the targeted medial thalamus – centrum medianum (CM). The CM was localized 4–6 mm lateral to the wall of the 3rd ventricle, 8 mm posterior to the mid-point and 3 mm superior to the intercommissural line. GT was performed by Leksell Gamma Knife with an applied dose ranging from 140 to 155 Gy; single shot, 4 mm collimator. Pain relief after radiation was evaluated. Decreased pain intensity to less than 50% of the previous level was considered as successful.

Results: Initial successful results were achieved in 8 (44.4%) of the patients, with complete pain relief in 1 these patients. Relief was achieved after a median latency of 5 months (range 2–36 months). Pain recurred in 4 (50%) of patients after a median latent interval of 24 months (22–30 months). No neurological deficits were observed.

Conclusions: Our results suggest that GT in patients suffering from severe pain syndromes is a relatively successful and safe

method that can be used even in severely affected patients. The only risk of GT for our patients was failure of treatment, as we did not observe any clinical side effects.

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#8555

A Multimodal Neurophysiologial Approach to Intraoperative Monitoring for Dorsal Root Entry Zone (DREZ) Lesioning for Neuropathic Deafferentiation Pain after Brachial Plexus Avulsion Injury

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Keywords: Neuropathic pain, Brachial plexus avulsion, Dorsal root entry zone.

Background: Dorsal root entry zone lesioning (DREZ) lesioning as a treatment of intractable neuropathic pain after brachial pleexus avulsion injury has proven to have long lasting pain relief (1). However, the safety and success of this method depends on accurate localisation of the DREZ. Difficulties in accurately localising the DREZ due to the lack of normal anatomy motivated the development of a neurophysiological techinique to identify the DREZ.

Methods: A multimodal approach was developed over a consecutive series of 22 patients. The method comprised spinal cord somatosensory evoked potentials with peripheral nerve stimulation and spinal cord motor evoked potentials. In addition, the integrity of the ascending and descending pathways was monitord during thermocoagulation radiofrequency lesioning with transcranial motor evoked potentials and somatosensory evoked potentials.

Results: The corticospinal tract and dorsal columns were located reliably using these methods thereby allowing identification of the lesion site lying between these two functional columns. Postoperatively, 90% of patients reported complete pain relief. 10% (2 patients) had partial pain relied and both were at the start of the series whilst the technique was being developed. One has been reoperated and is now pain free. The median follow up period after surgery was 18 months. There were no long term complications but there were transient lower limb clumsiness and numbness reflecting mild dorsal column loss.

Conclusion: A multimodal neurophysiological approach improves the accuracy of localising the DREZ for thermocoagulation lesioning in the treatment of neuropathic deafferentiation pain after brachial plexus avulsion injuries. The results were excellent and long lasting with minor side effects. This continous monitoring provides the additional safety needed to create adequate leaiosn reflected by these good results.

#8568

Longterm Follow-Up of Bifocal Thalamic Deep Brain Stimulation for Treatment of Chronic Neuropathic Pain

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Background: Longterm follow-up of bifocal thalamic deep brain stimulation for treatment of chronic neuropathic pain Mahmoud Abdallat, Andreas Wloch, Hans E. Heissler, Assel Saryyeva, Joachim K. Krauss Klinik für Neurochirurgie, Medizinische Hochschule Hannover, Carl-Neuberg-Str. 1, 30625 Hannover.

Objective: To assess long-term efficacy of deep brain stimulation (DBS) for chronic neuropathic pain in consecutive patient.

Methods: Patients with chronic neuropathic pain which were refractory to medication underwent bifocal thalamic implantation of DBS electrodes. Targets were the centromedian parafascicular nucleus (CM-Pf) and somatosensory thalamus (either nucleus ventralis postereolateralis, VPL, or ventralis postereomedialis, VPM) Elektrodes were implanted by CT-stereotactic surgery and externalized for 4–14 days to assess the effect of the two targets and to decide whether chronic stimulation could be administrated. Therefore DBS electrodes were either removed or a pulse generator was implanted. Assesment of pain included VAS scores and patient self rating. Patients were follow-up regularly at annual visits on longterm.

Results: Over a period of 16 years, a total of forty patients (20 women, 20 men; mean age of surgery 53.8 years, range 24–73 years) underwent bifocal implantation of thalamic DBS electrodes. Impulse generator were implanted in 33/40 patients for chronic stimulation, while 7 patients did not a chieve adequate benefit during test stimulation. Three patients were lost to follow-up in longterm followup, and in five patients the neurostimulation system was explanted due to infection. On longterm 20/33 had chronic CM-Pf stimulation and 13/33 had VPL/VPM stimulation. In three patients, the target was changed through the years or both electrodes were stimulated in parallel. The properties of marked/excellent vs. moderate/minor vs. no improvement was similar with both targets in longterm follow-up according to patient self-rating.

Conclusions: Pain pathway pass through thalamic relay, it is quite unclear, however, which thalamic nuclei would be the optimal targets for chronic stimulation (paleo-/neo-spinothalamic tracts). Good improvement of pain after DBS in the both of targets and no significant difference between CM-Pf and VPL as a good target of DBS for pain. There is significant reduction of analgesics after DBS.

#8592

Tibial Nerve Stimulation with a Miniature Wireless Stimulator in Chronic Peripheral Pain

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Keywords: Tibial nerve stimulation, Peripheral nerve stimulation, Miniature stimulator, Peripheral neuropathic pain, Complex regional pain syndrome.

Peripheral neuropathic pain (PNP) and Complex Regional Pain Syndrome (CRPS) can be effectively treated with peripheral nerve stimulation (PNS). In this case series report effectiveness of novel, miniature, wirelessly controlled microstimulator of tibial nerve (BlueWind, Israel) in PNP and CRPS was evaluated. In this pilot study the follow-up was 6 months in 6 patients, the average preoperative VAS was 7.5, after 1 month was 2.6 ($p = 0.03$), after 3 months was 1.6 ($p = 0.03$), and after 6 months average VAS score was 1.3 ($p = 0.02$). Mean average score in 6 patients during a week preceding baseline visit was 7.96, preceding 1 month visit 3.32 ($p = 0.043$), preceding 3 months visit 3.65 ($p = 0.045$), preceding 6 moths visit was 2.49 ($p = 0.002$). Average SF-McGill pain score before surgery was 23.8, after 1 month 11.0 ($p = 0.45$), after 3 months was 6.3 ($p = 0.043$), after 6 months 4.5 ($p = 0.01$). Applied therapy caused reduction of pain immediately after its application and therapeutic effect was observed in the 1st and the 3rd months till the 6th month on similar level in all patients. No complications of the treatment were observed. Intermittent tibial nerve stimulation with the use of novel, miniature, wirelessly controlled device can be effective and feasible in PNP and CRPS. It is a safe, minimally invasive and convenient neuromodulative method.

#8601

Outcome after Microvascular Decompression for Trigeminal Neuralgia Due to Venous Neurovascular Conflicts: In a Series of Consecutive Patients

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Introduction: Venous compression is not considered a classical cause of trigeminal neuralgia. Outcome after decompression of such neurovascular conflicts has not been yet thoroughly studied. The objective of this study is to describe the clinical characteristics and outcome in a series of patients with classical TN due to venous compression.

Material and Methods: All patient with suffering from TN treated by microvascular decompression (MVD) from 2005 to 2013 were included if a significant venous compression was found at the surgery. Patients were evaluated for clinical presentation, operative findings and the long-term outcome. Patients were considered as successfully treated for their trigeminal neuralgia if they were classed as BNI I or II. Kaplan-Meier analysis was used to determine probability of success at ten years follow up.

Results: Out of 313 patients having been treated by MVD during the study period in 55 (17.5%) a vein was the main compressive vessel, in 26 (8.3%) it was the only compressive vessel. Probability of relief with no need for medication at ten years was 70.6%. The patients with focal arachnoiditis had a poor long term outcome BNI III-V 71% compared to 14.5% without ($p = 0.0037$ Fisher's exact test). Degree of compression did not significantly influence outcome. No differences in outcome were found between patient presenting purely venous compression and mixed venous and arterial compression. Atypical trigeminal neuralgia and degree of compression were not prognostic factors in this series.

Conclusion: Venous neurovascular conflict as a cause of trigeminal neuralgia is far from rare. Microvascular decompression in cases with evident compression on imaging studies gives a good probability of pain relief encouraging to propose surgery for such patients.

#8609

Intrathecal Ziconotide for the Treatment of Sever Chronic Refractory Neuropathic Pain Due to Spinal Cord Lesions

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Keywords: Ziconotide, Neuropathic pain, Spinal cord lesions.

Introduction: Neuropathic pain due to spinal cord lesions is notoriously difficult to treat with little or no therapeutic options in particular for sublesional Ziconotide a N type-calcium channel blocker with selective action on the pain somatosensory system was approved for the treatment of severe chronic pain of various origins (cancer, neuropathic) since 2005. pain. Its use is exclusively intrathecal with potentially severe side effects. In a pilot study, we aimed to test the efficacy and side effects of Ziconotide in patients with severe refractory neuropathic pain of spinal origin. The main objective was to assess the analgesic effect of Ziconotide on the VAS and tolerance after a year of use.

Population-Method: Eleven adult patients, 8 men, 3 women with spinal cord lesions were included (post-traumatic injury, ischemic, syringomyelia, tumoral). Initial tests were made by lumbar puncture (1 to 3 mg). In cases of an inconclusive test, an alternative test with a lumbar continuous and progressively increasing infusion through an external pump (from 1 to 10 ug/day) was performed. Responders (VAS decreased >2 points/10) without side effects were implanted with a continuous infusion pump. Follow up patients is 12 months minimum. Outcome measures at 12 months were decrease in VAS, patient satisfaction and major side effects.

Results: Baseline VAS was measured at 6.83/10. Tests were preformed in all patients either by LP or by continuous infusion. In three patients the LP test was not performed due to the presence of Cerebral Spinal Fluid (CSF) block at the lesion level and.

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Overall 8 patients were considered responders to an average dose of 2.81 μg/24 hours. In three patients severe side effects were noted (2 CPK increases, retention of urine). Five patients received long term treatment with ziconotide and were evaluated at one year. A decrease in the average VAS 5.8/10 as well as a significant reduction in their oral analgesic treatment at one year follow up (average dose = 7.2 μg) were observed. Out of the five patients four considered the treatment to significantly impact their pain.

Conclusion: Ziconotide alone can beneficially impact neuropathic pain in a very specific and refectory group of patients when appropriately selected and tested. Further improvements in selection, testing and delivery methods might increase number of responders and efficacy of the treatment.

#8616

Long-Term Effects of Third Ventricle Deep Brain Stimulation in Cluster Headache

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Keywords: Deep brain stimulation, Cluster headache, Third ventricle.

Despite the increasing number of pain relieving therapies, and the progresses made in headache treatment, about 20% of Chronic Cluster Headache suffering patients are still resistant to drugs. This form of Trigeminal Autonomic Cephalalgia is one of the cruelest pains ever described, consisting of extremely severe unilateral pain attacks in the orbitotemporal region accompanied by ipsilateral autonomic symptoms. Deep Brain stimulation (DBS) of the posterior hypothalamus (pHyp) was the first surgical technique introduced to prevent attacks, followed by Occipital Nerve Stimulation (ONS) and Sphenopalatine Ganglion stimulation (SPG). Open studies on pHyp stimulation have shown some efficiency, although the mechanism of its efficacy is still not clear. One of the most attractive hypothetic effects is the modulation of the mesencephalic grey substance or of its neighboring third ventricle's floor structures. We already described an alternative technique consisting in intraventricular stimulation of the floor of the third ventricle. We report here the results at long term follow-up of the whole series of patients operated at Grenoble University.

Eleven patients diagnosed with intractable Chronic Cluster Headache, aged from 24 to 60 years, were enrolled in a prospective open study. Four out of 11 failed Occipital Nerve Stimulation (ONS). One patient received ONS 76 months after hypothalamic DBS. A single electrode was laid on the floor of the third ventricle. The number of attacks was collected at baseline and at 3, 6, 12 months postoperatively, then at long term (9–113 months). In addition to physical and laboratory monitoring, patients' mood was regularly assessed.

Besides establishing the feasibility and safety of the technique, this study reports the long term efficacy of third ventricle stimulation in reducing the number of headache attacks: 3/11 patients are pain free or have >80% improvement, 5/11 have >50% improvement, 1/11 show lesser improvement, while 2/11 have no significant improvement. Anxiety and Depression scores are also significantly ameliorated. No severe adverse events have been reported so far.

This technique could be a surgical alternative when all techniques have failed to treat iCCH. It has shown efficacy, although it appears to progressively dampen its impact in some patients.

#8763

Cervical and High-Thoracic Dorsal Root Ganglion Stimulation (DRG) in Chronic Pain

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Keywords: DRG, CRPS, Cervical pain.

Introduction: Dorsal root ganglion is a promising new target in neuromodulation of chronic pain states of different origin. Commonly used in the lumbar region, DRG can be used in the upper thoracic and cervical region with slight alterations of the surgical approach. Data on outcome and complications rates of DRG in this region are limited.

Methods: We report on a consecutive series of 11 patients treated with DRG stimulation (Spinal Modulation®) in the upper thoracic and cervical region. All patients suffered from chronic pain due to peripheral nerve or brachial plexus injuries, spinal cord surgery, post-herpetic neuralgia or CRPS II. All patients were trialed with externalized electrodes for 3–7 days; a successful trial was defined as at least 50% pain reduction.

Results: Out of all 11 patients trialed, 9 were successfully trialed and implanted with a permanent stimulation system. Two patients had one electrode implanted, all other were implanted with two electrodes in adjacent segments. Of the finally implanted patients, all but one patient (suffering from post-herpetic neuralgia) reported permanent clinical significant pain reduction (VAS reduction from mean 8.1 to 2.3). Loss of treatment effect requiring reprogramming was commonly observed during the first few month of treatment. In one patient a transient paresis of the arm and hand was observed immediately following electrode implantation.

Conclusion: Cervical and upper thoracic DRG stimulation is feasible and resulted in good overall response rates to trialing and excellent long-term pain relief in primary responders. A modified approach has to be used when compared with lumbar DRG electrode placement. Surgery itself in this region is more complication prone and challenging. Best results were seen in patients with brachial plexus and peripheral nerve injuries.

#8765

Burst or Tonic Stimulation? Results of a Placebo Controlled, Double Blinded, Randomized Study for the Treatment of FBSS Patients – 2y Follow-Up

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Keywords: Burst stimulation, SCS, Pain, FBSS.

Introduction: Spinal cord stimulation is an established method for treatment of chronic pain in FBSS patients. In the last decades only tonic stimulation patterns were used to modulate the pain. There were several reports that indicate that burst stimulation offers other opportunities and advantages. The goal of this study was to evaluate the pain level during placebo stimulation, burst stimulation, 500 Hz tonic stimulation with tonic 40–50 Hz stimulation as a baseline and to show long-term outcome among this population.

Materials/Methods: The study was designed as a double blind, randomized, prospective, cross over study. 20 patients were enrolled and completed the study at the investigational site. The patients were randomized to one of six treatment sequences. Twenty patients with FBSS and a pre-existing SCS system each received 3 treatment allocations in random order for a period of 1 week: Tonic 500 Hz Stimulation, Burst Stimulation, and Placebo Stimulation.

Results: The primary outcome measure was overall pain intensity measured on a numerical rating scale (NRS), 6.9 (baseline) vs. 4.2 (tonic) ($p < 0.001$), tonic vs. 2.08 (burst) ($p < 0.001$). Secondary outcome measures were pain quality measured using the Short Form McGill Pain Questionnaire (SFMPQ). Additional data were collected relating to pain related disability measured using the Oswestry Disability Index (ODI). Mean overall NRS and SFMPQ scores were not significantly different between Tonic 500 Hz Stimulation and Placebo Stimulation. Although the lowest mean ODI score was observed under Burst Stimulation, no significant differences were found between the ODI categories. No adverse events occurred, and Burst Stimulation was significantly preferred by 17 patients (80%). Positive results sustained during the long-term follow up. After two years mean VAS score under burst stimulation was 3 (range 0–6) ($p < 0.001$), 1 pat. died, 1 was lost for FU, 1 suffered from stroke and was switched off.

Conclusions: The lowest mean NRS and SFMPQ scores were observed under Burst Stimulation. For the Burst Stimulation treatment group, mean NRS and SFMPQ scores were significantly decreased compared with the other treatment groups. Overall, Burst Stimulation resulted in significantly better constant pain relief and improved pain quality during the 2 y follow-up.

#8767

Technical Aspects of SPG Stimulation for Cluster Headache: A New Frontier in Neuromodulation

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Keywords: Pain, Cluster headache, SPG stimulation.

Introduction: Cluster headache (CH) is a debilitating, severe form of headache. A novel non-systemic therapy has been developed that produces therapeutic electrical stimulation to the sphenopalatine ganglion (SPG). Our experiences with a transoral surgical technique for inserting the Pulsante SPG Microstimulator into the pterygopalatine fossa (PPF) are presented herein.

Methods: We implanted 5 CH pats so far, 3 females, 2 male. 2 out the total already received an ONS device with partial (30% seizure reduction) long-term effect. Technical aspects include detailed descriptions of the preoperative planning using computed tomography scans, 3D printouts of the individual skull base for presurgical digital microstimulator insertion into the patient-specific anatomy and intraoperative verification of microstimulator placement. Surgical aspects will be presented including techniques to insert the microstimulator into the proper midface location atraumatically.

Results: 4 weeks after implantation stimulation was switched on, patients are asked to stimulate 15 minutes during the attacks. All patients benefit from surgery so far. The 2 combined ONS/SPG patients where almost free of attacks. The further 3 patients reported (preliminary 6–8 weeks after OR) already an improvement including a reduction of attack duration and severity. One surgical complication occurred with misplacement of the electrode into the ethmoidal sinus. By using intraoperative CT this was immediately revised and ended in an accurate final electrode position.

Discussion: Our personal experience with this new technique and the results of our patients fit in the findings so far reported in the literature. During the Pathway CH-1 and Pathway R-1 studies, 99 CH patients received an SPG microstimulator. Ninety-six had a microstimulator placed within the PPF during their initial procedure. Perioperative surgical sequelae included sensory disturbances, pain, and swelling. Follow-up procedures included placement of a second microstimulator on the opposite side ($n = 2$), adjustment of the microstimulator lead location ($n = 13$), replacement after initial unsuccessful placement ($n = 1$), and removal ($n = 5$). This SPG microstimulator insertion procedure has sequelae comparable to other oral cavity procedures including tooth extractions, sinus surgery, and dental implant placement. Twenty-five of 29 subjects (86%) completing a self-assessment questionnaire indicated that the surgical effects were tolerable and 90% would make the same decision again.

Conclusion: SPG is safe and feasible. We hereby present the technique and preliminary personal results of this new approach for a debilitating disease. With an interdisciplinary team technical limits can easily be solved. Further studies are required regarding long-term efficacy of this promising method.

Psychiatric Disorders

#8015

Using Simultaneous DBS/EEG Recordings to Understand the Circuitry Underlying Neuropsychiatric Disorders

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Keywords: Oscillations, Large-scale networks, Granger causality, Obsessive compulsive disorder, Tourette syndrome.

Neuropsychiatric disorders are prevalent in society. It is reported that at least 38% of Europeans suffer from them presently and that three out of five Europeans will suffer from a brain disorder in the next twenty years. Despite the pervasiveness of these illnesses and the great personal, financial and societal burden which clearly accompanies them, our understanding of the biological basis of these disorders is severely limited. In the search for the underlying neuropathomechanisms of these, a commonality has emerged. Pathological oscillations have been nearly ubiquitously associated with the dysfunctional brain states associated with these disorders.

Deep brain stimulation (DBS) is a relatively new therapy which has enjoyed successful application and approval for several neurological disorders. It is suggested that DBS substantially reduces refractory symptoms in these disorders via the modulation of dysregulated networks. This theory is supported by the reports of correlation between improved symptomatology and the observed changes in synchronization of oscillatory rhythms. Although these data consequently suggest an important role for oscillatory rhythms, the scope of these rhythms in the pathological network and the mechanisms which exact their modification in the improved disease state has yet to be determined. Such information would bear directly on the important issues, including that of target selection.

In order to examine the functional relevance of oscillations in the context of the large-scale networks of the brain, we combined neurophysiological recordings from subcortical targets in Gilles de la Tourette syndrome (GTS) or obsessive-compulsive disorder (OCD) with cortical recordings from the scalp in a cohort of males and female patients (27–55 years old) selected for DBS therapy. Electrophysiological recordings were taken post-operatively during the resting state from externalized DBS electrodes bilaterally implanted in the centromedian nucleus of the thalamus or the nucleus accumbens, respectively. These were simultaneously recorded with multi-channel scalp EEG. We investigated Granger-causal relations among these multivariate time series by employing directed functional connectivity measures using generalized partial directed coherence. In all patients, distinct subcortical electrodes (bipolar derivates) were identified as drivers of the large-scale subcortical-cortical networks at specific frequency ranges. Furthermore, these projected to circumscribed electrode sites on the scalp. In turn, particular scalp electrodes projected to the subcortical structures. Importantly, the subcortical and cortical electrodes had different preferred frequencies of communication. The data from these cortical-subcortical simultaneous recordings explore the mechanism of communication in the large-scale pathological networks of GTS and OCD. By uncovering the contribution of the deep as well as cortical structures to the network, a more comprehensive understanding of the circuitry of not only these disorders in particular, but also of neuropsychiatric disorders in general, is feasible. Such circuit-level understanding could power a shift in the search for the 'silver-bullet' target in these disorders as well as lead to new concepts in the identification of biomarkers for neuropsychiatric diseases.

#8040

Thalamic Deep Brain Stimulation for Refractory Tourette Syndrome: Clinical Evidence for Increasing Disbalance of Therapeutic Effects and Side Effects at Long-Term Follow-Up

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Keywords: Tourette syndrome, Deep brain stimulation, Thalamus.

Introduction: Tourette Syndrome (TS) is a chronic childhood-onset neurodevelopmental disorder characterized by multiple motor and vocal tics. Deep Brain Stimulation (DBS) of different targets within the basal ganglia has emerged as a therapeutic option for refractory TS patients. DBS of the medial thalamus has proven to be effective in reducing tics at the short-term. This paper details the long-term outcome of seven refractory TS patients.

Methods: Seven patients underwent bilateral DBS between 2001 and 2008 in our centre. The target was the centromedian nucleus–substantia periventricularis–nucleus ventro-oralis internus cross point of the thalamus. During visits to the outpatient clinic the effect on tics, side effects, complications and stimulations parameters were evaluated. The effect on tics was measured using the Yale Global Tic Severity Scale (YGTSS). Follow-up duration was variable, ranging from 12 to 78 months.

Results: Patient 1 showed an improvement of 81.6% on the YGTSS after 60 months, but after some years he needed higher voltage stimulation to suppress the tics. Side-effects (i.e. reducing levels of energy and visual disturbances) became more severe and the target was changed to the anterior part of the internal pallidum. Unfortunately he was not satisfied with the effects of the pallidal DBS and after some years he decided to turn the thalamic leads on again and accept the side-effects.

Patient 2 developed a postoperative vertical gaze paralysis due to a small bleeding at the tip of the left electrode. The YGTSS improved 56.8% at 12 months of follow-up and this improvement persisted till 36 months of follow-up. Although the vertical gaze paralysis resolved, he continued having visual disturbances and pressure behind his eyes during stimulation. Due to these side effects and the burden of visiting the outpatient clinic, he eventually decided to switch the stimulator permanently off.

Patient 3 is still satisfied with the effects of the DBS. Tics progressively diminished after surgery and the YGTSS improved till 88.9% at 78 months of follow-up.

Patient 4 experienced a tic improvement of 34.8% on the YGTSS after 16 months. Side-effects (i.e. reduced levels of energy and visual disturbances) became more pronounced over time, and when the whole system had to be removed due to a persisting hardware infection after six years, the target was changed to the anterior part of the internal pallidum. With pallidal DBS an improvement of 64.5% on the YGTSS was observed after 12 months.

Patient 5 showed a minor tic improvement of 27.5% on the YGTSS after 12 months. He was discontent, went to Belgium for stimulation of the external globus pallidus and was lost to follow-up.

Patient 6 showed a tic improvement of only 34.1% on the YGTSS after 26 months. Moreover, he developed various symptoms like binge eating, lethargy, dysarthria, gait disturbances and apathy. A CT-scan performed six months after surgery revealed cerebellar atrophy, not present at preoperative imaging. Due to all these other symptoms and the lack of effect we turned the stimulator off and he was lost to follow-up.

Patient 7 showed an improvement of 39.5% on the YGTSS after 8 months. Major adjustments in stimulation parameters were needed, however he still suffered from serious side effects (i.e. reduced levels of energy, gaze disturbances, alteration of sexual function). After 5 years only 9% tic improvement sustained and after 9 years a hardware defect in the left electrode was found and the whole system had to be removed. The target was changed to the anterior part of the internal pallidum. With pallidal DBS he experienced an improvement of 80.4% on the YGTSS after 38 months of follow-up, without experiencing serious side-effects.

Conclusion: In patients receiving thalamic DBS for refractory TS there seems to be an increasing disbalance of therapeutic effects and side effects at long-term follow-up, often leading to either switching off the stimulator or new surgery with a different neuro-anatomic target (the anterior part of the internal pallidum). The reported cases reflect the strong heterogeneity of the disease and comorbidity, the impact of expectations and ambitions, all interfering with effects and side-effects and in the end satisfaction with DBS.

#8489

Chronic DBS Stimulation of Minimally Conscious State: Methodological Issues

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Keywords: DBS, Consciousness, Brain injury.

Introduction: The modulation of consciousness processes with deep brain stimulation (DBS) in minimally consciousness state seems achievable. Between 1968 and 2016 nine teams have reported effects in 58 vegetative (VS) or minimally conscious (MCS) patients. We analyzed the literature focusing on methodological issues, willing to address clinically relevant key-points for the selection of targets and design of future studies.

Literature Review: Half of the studies were case-reports. Most teams intended to place electrodes in the thalamus. All leads were implanted according to atlas-based coordinates. Five studies used low frequency stimulation, 25 to 50 pulses/sec, and three high frequency stimulation, at 100 and 250 pulses/sec. The most recent studies reported effects in continuing VS-MCS patients, followed up during several months or years. The clinical status and DBS effects were measured using simple clinical observations, up to JFK Coma Recovery Scale–Revised. Parallel to the clinical status, the most recent study analyzed the extent of brain lesions. No severe irreversible, stimulo-induced, adverse effects were reported, but one patient had post-operative intra cerebral hematoma. One clinical study had double-blinded on/off crossover phase, whereas the others were observational studies. From these studies it can be inferred that high or low frequency stimulation of deep gray structures, particularly of the central thalamus, can provoke overt conscious behaviors. Recent literature concerning models of consciousness related circuitry let us think that several deep brain regions and cortices are involved and could be future relevant spots of neuromodulation.

Conclusion-Perspective: Future studies willing to modulate the deep brain circuitry should take into account the recent knowledge on altered dynamics of neural correlates of disorder of consciousness, the dynamics of spontaneous recovery, and the consequences of structural and functional lesions.

#8511

Deep Brain Stimulation of the Subthalamic Nucleus Reduces Motivation for Cocaine While Increasing That for Apple Sauce in the Monkey

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Keywords: Addiction, Psychiatry, Neuromodulation.

There is currently no pharmacological treatment for cocaine addiction, therefore it's important to look for alternative treatment strategies. One possibility could be a surgical approach.

Indeed, it has been shown in the rat that the inactivation of the subthalamic nucleus (STN), by either lesions or high frequency Deep Brain Stimulation (DBS), reduces motivation for cocaine while increasing motivation for food. It has thus been suggested that STN high frequency DBS could be a good strategy to treat cocaine addiction. Before testing in human addicts, the aim of the present study was to validate this hypothesis in non-human primates. We have trained two monkeys to work under various schedules of reinforcement (Fixed Ratio 15 (FR15) and Progressive Ratio (PR)) for either apple sauce or cocaine (intraveinous 0.1 mg/kg/injection).

After stabilisation of performances, electrodes have been implanted bilaterally in the STN, and chronic stimulation has been further applied (130 Hz, 2 V). All conditions (apple saucestimulation ON, apple sauce-stimulation OFF, cocaine-stimulation ON, cocaine-stimulation OFF) have been tested in alternance. Results have first shown that the level of motivation was higher for cocaine than for apple sauce before stimulation. Then, after STN DBS, the motivation for apple sauce was significantly increased while that for cocaine was significantly decreased. These results confirm the opposite effect of STN DBS on motivation that has been previously demonstrated in rats. Since decreasing the motivation for the drug, without diminishing other forms of motivation is the goal for a possible treatment of cocaine addiction, STN DBS may thus be the appropriate strategy.

#8525

Closed-Loop Brain Stimulation for Psychiatric Disorders: Evidence from Rodent and Human Studies

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Keywords: Deep brain stimulation, Psychiatric disorders.

This is the abstract from the recipient of the 2014 ESSFN Research Grant, Dr. Hemmings Wu, for the 30-minute presentation before closing ceremony.

Neurosurgical intervention, such as deep brain stimulation, is an effective treatment of last resort for selective otherwise-refractory psychiatric disorders, including obsessive-compulsive disorder, major depressive disorder, Tourette Syndrome, and anorexia nervosa. While its mechanisms involve modulation of underlying neurocircuitries, it is essentially acting without receiving any neural feedback. Such continuous high-frequency electrical stimulation can lead to side effects due to excessive stimulation, decreased efficacy due to neural adaptation, and shorter battery life. Closed-loop brain stimulation, where electrical stimulation is delivered only when needed, is the emerging new technology to resolve these issues. Preliminary animal and human trials have shown promising results in Parkinson's Disease.

But in order to achieve closed-loop brain stimulation for psychiatric disorder, a robust real-time neural biomarker of the key psychiatric symptom must first be identified. In this presentation, we will first demonstrate the neural biomarkers, in the form of local field potentials, recorded through implanted microelectrodes, discovered in two different rodent models of compulsion and loss-of-control behavior in the bed nucleus of the stria terminalis and the nucleus accumbens. We then put these biomarkers to test, to examine their sensitivity and specificity, and their robustness as closed-loop stimulation biomarkers. Lastly, we will present evidence from human studies, and discuss the translational potential of our findings.

#8529

Deep Brain Stimulation for the Early Treatment of the Minimally Conscious State and Vegetative State. Experience in 14 Patients

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Keywords: Minimally conscious state, Vegetative state, Deep brain stimulation, Centromedian-parafascicular nucleus.

Introduction: An effective treatment of patients in a minimally conscious state (MCS) or vegetative state (VS), caused by hypoxic encephalopathy (HE) or traumatic brain injury (TBI), is not yet available. Deep brain stimulation (DBS) of the thalamic reticular nuclei, as a therapeutic procedure, has been attempted mainly in patients with TBI.

Methods: Fourteen out of 49 patients were included in this study (4 patients had TBI and 10 patients had HE, 4 being in MCS and 10 patients in VS). The selection criteria for DBS, evaluating status of cerebral cortex and thalamocortical reticular formation, included: neurological evaluation, electrophysiological evaluation and the use of imaging techniques such as positron emission tomography (PET) and magnetic resonance imaging (MRI). The target for DBS was the centromedian-parafascicular nucleus (CM-pf) complex. Patient follow-up was between 38 and 60 months.

Results: Two MCS patients regained consciousness and regained their ability to walk, to speak fluently and live independently. One MCS patient reached the level of consciousness, but currently is still in a wheelchair. One vs. patient (after cerebral ischemic lesion) improved to the level of consciousness and currently responds to simple commands. Three vs. patients died from respiratory infection, sepsis or cerebrovascular insult, respectively. Other patients remained without substantial improvement of consciousness.

Conclusion: The spontaneous recovery of MCS vs. to the level of consciousness with no or minimal need for assistance in everyday life is very rare, therefore if a patient is a candidate according to the above mentioned criteria, DBS could be a treatment option.

#8534

The Proper Target for OCD DBS Is Individualized for Each Patient Along the Striatum Depending on the Content of the Obsessions

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Introduction: Although different targets are used to treat obsessive-compulsive disorder (OCD) with deep brain stimulation (DBS), the overall results (about 50% of responders) have not improved from the lesion-making era. Probably this is because OCD is a heterogeneous disease, with different symptomatic dimensions. We hypothesized that the optimal target is individualized for each patient, related to the symptomatic dimension. Further, we tested the possibility to use functional and structural connectivity to predict it.

Material and Methods: We conducted a prospective, randomized, double blinded study in seven OCD patients. A fMRI Maudsley's test showing pictures related to several symptomatic OCD contents was performed. Then, the striatum was segmented using the projections of ventromedial, orbitofrontal, dorsolateral and anterior cingulate cortices. A tetrapolar electrode (Medtronic ****) was inserted along the striatum using a trajectory in which each contact was closest to each segment. Patients were stimulated using a random series of five periods (four contacts plus a zero volts activation) during three months, separated by one month washout period. Patients were evaluated for clinical and neuropsychological effects by an observer blind to the active contact.

Results: Six patients (85.71%) were responders to any contact, with a mean YBOCS reduction of 50.84%, while only three (42.86%) responded to the most distal contact, (mean YBOCS reduction: 21.69%). Patients showing obsessions and compulsions related to body danger responded best to the more ventral contacts (two cases), while those showing symptoms with ideatory contents or those related to checking (or ordering) responded best to more dorsal contacts. We found a relationship between the volume of tissue activation in each contact and the tracts crossing from the cortical activated area after the Maudsley's test towards the striatum.

Conclusion: These results suggest that there is an individualized proper DBS target depending on the contents of obsessions in OCD patients.

#8554

Deep Brain Stimulation of the Internal Capsule/Nucleus Accumbens for Obsessive-Compulsive Disorder: Where Is the Best Target?

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Keywords: Obsessive-compulsive disorder, Deep brain stimulation, Nucleus accumbens.

Introduction: Obsessive-compulsive disorder (OCD) is a psychiatric disorder characterized by recurrent persistent thoughts known as obsessions, and time-consuming ritualistic behaviors known as compulsions. Cognitive behavioral and pharmacological therapies may be required when symptoms interfere with the global functioning of the patient. However, up to 10% of OCD patients treated with these therapies show an insufficient improvement of symptoms. For those patients, surgery may be considered. Several targets have been implicated in the study of the effects of deep brain stimulation (DBS) on OCD symptomatology. The most common targeted areas are the nucleus accumbens (Nacc), the internal capsule (IC), the ventral capsule/ventral striatum, and the subthalamic nucleus. To these days, there is still an ongoing debate about the best target for DBS in OCD patients. Furthermore, these structures cannot be considered as completely distinct targets as the NAcc is located immediately underneath the anterior limb of the IC and extends dorsolaterally into the ventral putamen and dorsomedially into the ventral caudate nucleus. Therefore, the differences between the position of contacts, within the same lead, may determine the clinical postoperative outcome. The objective of this study was to determine the association and differences between location of active contacts within the Nacc and the ventral IC and clinical outcome at long-term follow up.

Methods: Twenty-three patients who underwent implantation of unilateral (N = 3) or bilateral (N = 20) electrodes for Nacc DBS were included in this study. OCD symptoms were measured with the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) scale before surgery and postoperatively for a long-term follow-up at different time points. For the lead location, preoperative MRI planning scans were fused with postoperative CT scans in order to assess the exact location of the active contacts in relation to the Nacc and the IC.

Results: The mean postoperative follow-up was 18 ± 7 months (range from 9–51 months). Mean stimulation parameters were 3.9 ± 1 V (range from 2.5–6.5 V), 96 ± 17 µs (range from 90–150 µs), 135 ± 7 Hz (range from 130–145 Hz). Patients with active contacts in the Nacc showed an average improvement on the Y-BOCS of 47%, whereas patients with active contacts located in the IC showed an average improve of 32%. However, if the active contacts were located within a maximumum distance of 1.5 mm of the transition between Nacc and the IC, the average improve on the Y-BOCS scores was of 58%.

Conclusions: OCD patients with active electrodes for DBS in the transitional zone between Nacc and IC showed the best clinical outcome on the Y-BOCS scores at long-term follow-up compared to active electrodes located in Nacc or IC. Further studies will be required to determine if different regions of the cortico-striato-pallido-thalamo-cortical network are activated during stimulation of region that could correlate with these clinical observations.

#8557

Development and Implementation of a WSSFN Psychiatric Neurosurgery Committee Lesion Registry

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Keywords: Ablative neurosurgery, Psychiatric disorders, Registry.

Despite the advent and popularity of high profile neurostimulation programmes, lesion surgery for psychiatric disorders is still performed in many centres around the world. For most centres, this is a low-volume activity and it remains challenging for any single centre to present compelling outcome data derived from large cohorts of treated patients. Similarly, it takes many years to collect data to test hypotheses relating to optimising patient selection, surgical technique and lesion topography. Globally, psychiatry, surgery, medicine, psychology and neuroscience communities, the media and the lay public tend to believe lesion surgery for psychiatric disorders is not only an outdated treatment approach, but also ineffective and harmful. Sporadic, small scale case series (n < 20) from single centres are unlikely to influence significantly wider opinion and practice.

Objective: To establish under the auspices of, and on behalf of, the Psychiatric Neurosurgery Committee of the WSSFN, an international, anonymised, pooled, clinical and neuroimaging dataset from centres offering ablative neurosurgery for Mood Disorders and Obsessive-Compulsive Disorder, and, where available, for other indications.

Aims: To build the capacity to compare retrospectively the clinical outcomes for different lesional procedures, across different clinical populations and across different international centres. Also, to establish the infrastructure for prospective collaborative audits of clinical outcomes framed around a shared, minimum dataset.

Method: Anonymised individual-level patient data will be hosted, on behalf of WSSFN, by the University of Dundee (Scotland, U.K) Health Informatics Centre (HIC), a component of the Farr Institute, a UK-wide, publicly funded research collaboration involving 21 academic institutions and health partners in England, Scotland and Wales. HIC is a secure, curated Safe Haven environment with robust data governance procedures for the provisioning of anonymous data to researchers for approved projects. Analyses are performed within the safe haven by approved investigators via secure remote access. The proposed initial 'ideal' dataset will include information acquired pre-surgery and at 12 m follow up re-

lating to patient demography, diagnosis, symptom severity and functional capacity alongside structural MR imaging – T1 and T2 weighted whole brain scans – stored in DICOM, ANALYSE or NIFTI format (where possible).

The inception date for the Registry is September 1st 2016 and the project will work to identify and collect suitable data for 12 months in the first instance. We seek expressions of interest from any centre wishing to collaborate.

#8758

Treatment of Medical Resistant OCD by Gamma Knife Radiosurgery

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Keywords: Obsessive-compulsive disorder, Radiosurgery, Gamma knife.

Obsessive compulsive disorder (OCD) is a challenging psychiatric condition. The authors evaluated their experience with Gamma Knife capsulotomy for treating patients with medical resistant and very severe OCD. A review of prospectively maintained data base was conducted for patients treated for untreatble OCD. Twelve patients were identified, Gamma Knife Radiosurgery with Elekta GK unit was used to target the anterior limb of the internal capsule bilaterally. Two 4 mm collimators shots was used in each side, maximun dose 120 Gy. All twelve patients were assessed preoperatively and postoperatively for clinical response by using both subjective and objective metrics; seven patients have postoperative neurorradiological follow up. the median clinical follow-up was 16 months (mean 32, 6–100 months). At the last follow-up nine patients showed good control of the obsessions and compulsions. One patient after a good response showed worsening and was considered a failure. Seven patients showed marked clinical improvement. the median YBOCS score was11 at the last follow-up. Neuroimaging with tractography confirmed the interruption of the internal capsule wich correlated with the clinical improvement. No adverse clinical effects were observed after radiosurgery.

Capsulotomy with GK is a promising and safe treatment for severe OCD cases. We discuss different items such aa anatomical localization of targets, dosimetry and follow-up of these patients.

#8781

EEG Resting-State Functional Connectivity Abnormalities in Patients with Obsessive-Compulsive Disorder

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Keywords: OCD, Granger causality analysis, functional connectivity.

Objectives: Obsessive-compulsive disorder (OCD) is one of the most disabling of all psychiatric illness with a lifetime prevalence of 2%–3% and an early onset in adolescence or young adulthood. Core symptoms of OCD are intrusive thoughts, feelings, or images (obsessions) and repetitive behaviors (compulsions) aimed at reducing anxiety associated with obsessions. Despite available pharmacological and psychotherapeutic treatments about 10% of OCD patients remain severely affected and are considered treatment-refractory. For some of these patients deep brain stimulation (DBS) offers an appropriate treatment method. In hopes of identifying better treatment options such as DBS, many attempts have been made to clarify pathological brain mechanisms. Alterations in brain functional cortical connectivity in resting-state networks have been detected with functional imaging techniques, but neurophysiological connectivity measures have not been systematically examined.

To address this question, we applied resting-state electroencephalography (EEG) to investigate the whole brain fundamental functional alterations in patients with OCD. In this study, we focused on oscillation-based functional connectivity.

Methods: We used the combined application of the independent component analysis (ICA) and the Granger causality (GC) analysis to examine resting state functional connectivity as measured by routine scalp-EEG in 10 patients with OCD and 10 healthy controls matched for age lying with eyes closed in a dark sound-attenuated room. After the power spectra was computed, GC spectra method, a part of spectral interdependency methods, was used to examine the strengths, directions, and frequencies of interactions between dynamic processes. The measures of spectral interdependency were derived from the time series recordings of dynamic systems by using autoregressive modeling. The direction of information flow between these EEG sources was then estimated using the directed transfer function (DTF).

Results: As compared to controls, the patients with OCD had decreased functional connectivity between medial prefrontal and occipital cortex, and between the left temporal and occipital cortex. The patients with OCD expressed lower information flow (DTF) in beta frequency range principally from the occipital to the medial prefrontal region, and from the occipital to the left temporal region.

Conclusions: We used resting-state EEG to study whole-brain functional connectivity patterns in patients with OCD and

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healthy controls. The primary finding was changed functional connectivity in large-scale networks including the medial prefrontal cortex, temporal cortex and occipital cortex in the patients with OCD. These results indicated EEG connectivity-based measurements could probably serve as reliable and valid biomarkers for diagnosis of OCD.

It has been suggested that deficits in the ability to selectively attend to relevant information while concurrently suppressing competing irrelevant information is a central feature of OCD. The impairment of inhibitory control in OCD patients might be reflected in abnormal cognitive functions, which seem to be due to reduced attention.

We speculate that decrease in functional connectivity in large-scale networks among the medial prefrontal cortex, temporal cortex and occipital cortex may be related to functional deficits in cognitive domains in OCD.

The impact of neurological and psychiatric diseases on the functional organization of the brain has been a topic of growing interest in the last decade. It is likely that most psychiatric disorders do not result from a deficit in a single brain area and that a network perspective is necessary to explain their complex etiology. OCD is associated with abnormal intrinsic functional connectivity in large-scale brain networks.

This network approach can shed some light on the pathophysiological mechanisms underlying neuropsychiatric disorders.

#8819

A Randomised Controlled Trial of Deep Brain Stimulation in Obsessive Compulsive Disorder: A Comparison of Ventral Capsule/ Ventral Striatum and Subthalamic Nucleus Targets

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Keywords: DBS, OCD, Psychiatry, Anteromedial subthalamic nucleus, Ventral anterior capsule.

Background: Obsessive compulsive disorder (OCD) has a lifetime prevalence of 1–2%. Standard treatments are ineffective in up to 40% of cases. Even with the best treatments, there remains a subgroup with severe symptoms and significant disability. Studies of deep brain stimulation (DBS) for OCD have shown improvement in both symptoms and quality of life in severe OCD. Two targets in particular have shown promise: the anteromedial subthalamic nucleus (STN) and the ventral capsule/ventral striatum (VC/VS) [1–3]. It is not clear however if one site has advantages over the other and, with regard to the VC/VS site, whether stimulation of the anterior capsule white matter or ventral striatum/nucleus accumbens grey matter is critical for improvement [2, 3].

Aims: We report a within subject comparison of the effect of DBS on OCD symptoms at STN and VC/VS sites both individually and together (ClinicalTrials.gov #NCT02655926). The aims of the study were to determine: a) the efficacy of DBS at each site; b) whether stimulation of both sites improves the response compared to either site alone; and c) the critical stimulation contacts at the VC/VS site.

Methods: Six participants, with severe treatment refractory OCD, were recruited via the UK specialist OCD service and underwent implantation of bilateral electrodes at both the VC/VS and anteromedial STN sites. A Leksell frame-based MRI-guided and MRI-verified approach under general anaesthesia was used. The subthalamic nucleus was localised on axial T2-weighted stereotactic images and the VC/VS localised on coronal and axial proton density images (Siemens, 1.5T). Using a double blind cross-over design, 12-weeks stimulation at STN and VC/VS sites was compared, followed by stimulation at both sites for 12 weeks. The primary outcome measure was YBOCS: an improvement of greater than or equal to 35% was the predefined response.

Results: Accurate stereotactic and anatomical lead location was confirmed on immediate postoperative stereotactic MR images in all patients. For the VC/VS target, the deepest DBS lead contact was within the nucleus accumbens, the one superior to that in the 'shell' of the nucleus accumbens while the superior two contacts were within the inferior aspect of the anterior limb of the internal capsule. The response rates (defined as the number of patients with >35% reduction in YBOCS) were: STN 3/6; VC/VS: 5/6; STN + VC/VS: 5/6. In the one non-responder YBOCS reduction was 32% after the combined STN+VC/VS stimulation phase. For the whole group, the mean reduction in YBOCS scores were: STN 16.3; VC/VS: 19.2; STN + VC/VS: 22.0 which represents a mean reduction of 42%, 53%, 62% from their own baseline scores and a reduction to predefined mild/subclinical symptoms of 0%, 50% 50% respectively. The top two DBS contacts of the quadripolar lead were found to be the most effective at the VC/VS target in all 6 patients.

Conclusion: These results suggest that: a) The VC/VS site may be superior to the STN site for the amelioration of severe OCD symptoms; b) There is only a modest advantage of stimulating both sites together; and c) The effective stimulation site for the VC/VS target is the inferior aspect of the anterior limb of the internal capsule and not the ventral striatum/nucleus accumbens grey matter.

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#8860

Deep Brain Stimulation (DBS) of the Superolateral Branch of the Medial Forebrain Bundle (slMFB) in Psychiatric Disorders – Surgical Technique

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Keywords: Major depression, Deep brain stimulation, DTI, tractography, slMFB.

Background: Deep brain stimulation (DBS) of the superolateral branch of the medial forebrain bundle (slMFB) emerges as an interesting alternative – yet experimental – treatment for therapy refractory psychiatric diseases. First experiences have been reported from a pilot trial in major depression (1) and an uncontrolled case series for obsessive compulsive disorder (OCD) (2).

Objective: To describe the surgical technique for deep brain stimulation (DBS) of the supero-lateral branch of the medial forebrain bundle (slMFB). To report our experience with the successful bilateral implantation in a larger patient group.

Methods: Surgical experience from bilateral implantation procedures in n = 27 patients is reported. The detailed procedure of diffusion tensor imaging magnetic resonance imaging fiber tracking (DTI FT) assisted targeting together with detailed descriptive electrophysiology in 144 trajectories of the target region (recording and stimulation) and intraoperative testing are addressed.

Results: In this early stage of experience, bilateral slMFB DBS requires DTI FT assisted targeting combined with in depth intraoperative electrophysiological investigation of the target region.

Conclusion: The slMFB is a promising target region for the treatment of some psychiatric disorders (1,2). DTI FT assisted DBS of the slMFB is based on an imaging technology that is readily addressed in other indications (3,4). To the authors' knowledge the slMFB is the only target region for psychiatric disorders that allows for intra-operative testing with clear effects and side effects to guide implantation. In our eyes, this makes surgery of the slMFB is in many features comparable to typical movement disorder surgery.

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#8863

Diffusion Tensor Magnetic Resonance Imaging Tractographic Analysis of slMFB DBS in Major Depression

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Keywords: Major depression, Deep brain stimulation, DTI, Tractography, slMFB, Outcome.

Introduction: The superolateral branch of the medial forebrain bundle (slMFB) is currently investigated as a putative DBS target for the treatment of major depression (MD) and OCD. Diffusion tensor magnetic resonance imaging tractography (DTI FT) assisted targeting is necessary. A total of 24 patients have so far been bilaterally implanted and stimulated for MD at our institutions in two IITs. Here we present a first analysis of this patient cohort focusing on the effectively stimulated fiber tracts and their connections with remote cortical and subcortical network structures via probabilistic DTI FT. Our hypothesis is that subcortical structures that belong to the reward system as well as cortical network structures (especially the prefrontal cortex), responsible for decision-making, goal directed behaviour, planning and mentalizing are affected through effective slMFB DBS (1).

Methods: Patient demographics: n = 24, 9f, 29–71 years (47.3 ± 10.5 years). All patients received bilateral DBS electrode through a stereotactic procedure (DBS 3389 model, Medtronic, USA). The procedure has been described in a previous study (2). Imaging data consisted of high-resolution anatomical MRI se-

quences (3T, Philips Intera, Best, Netherlands, T1W and T2W high resolution images) and 32-direction diffusion tensor imaging. Postoperative helical CT scans were used to delineate electrode positions.

The eddy current-induced distortions in diffusion images were corrected using the eddy-correct algorithm in FSL (www.fmrib.ox.ac.uk/fsl). The B0 image was extracted and used as a reference image for the postoperative T2W using FSL linear registration tool, FLIRT. The registered T2W was normalized into MNI space and segmented into GM, WM, and CSF using SPM12 (http://www.fil.ion.ucl.ac.uk/spm/software/spm12/). The CT was registered into the T2W in the B0 space using FLIRT. The individual effective contact locations were identified. Based on the identified coordinates, a spherical volume of interest (VOI) was created (typically with a radius of 3 mm, representing the volume of activated tissue [VAT]). A displacement field was applied on these VOIs. Probabilistic streamline tractography was performed with MRtrix 3 (http://www.mrtrix.org/). Generated tracks were further employed to convert a 3D image. The group average image was created and smoothed using a Gaussian kernel having a full-width at half-maximum (FWHM) of 4 mm.

Results: The clinical results of the patients have in part been presented previously (2). In the present study, a total of 21 data sets had sufficient quality for further evaluation. In all cases only the slMFB and not the inferomedial branch of the medial forebrain bundle (imMFB) where included in the VAT, as expected. On the group level (not normalized), fibers that were affected by DBS connected bilaterally to the nucleus accumbens, the corpus callosum and the medial prefronal cortex (BA 24 and 32). The strongest connection was seen with the rostral prefrontal cortex (BA10) and BA46 (but only before normalizing data).

Conclusion: The presented data supports the modulation of a widespread network containing the rostral prefrontal cortex and parts of the forceps minor and the medial prefrontal cortex in slMFB DBS together with subcortical structures of the reward system. BA10 is a unique part of the human brain and has important functions in decision making, multi-tasking and retrieval of episodic memory. Involvement of this region has also been described before with cg25 as target regions (3). BA10 might represent a common denominator for antidepressant efficacy. A combined modulation of the above described cortical and subcortical structures might explain the short and long-term clinical effects that are seen during DBS of the slMFB in MD (2).

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#8864

A Sham-Controlled Study of Deep Brain Stimulation to the Superolateral Medial Forebrain Bundle (slMFB DBS) for Treatment-Resistant Depression

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Keywords: Major depression, Deep brain stimulation, slMFB, Outcome.

Background: Several targets are currently investigated for their antidepressant efficacy in treatment resistant depression (TRD). Among them, DBS to the supero-lateral branch of the medial forebrain bundle (slMFB) lead to rapid and long-term antidepressant effects (1). We designed a larger study with a staggered onset sham-controlled design.

Methods: Sixteen patients suffering from TRD were treated with DBS bilaterally to the slMFB. Patients were either stimulated with DBS immediately (group A) or with a delay of two months (group B) (staggered onset) in a double blind protocol.

Outcome criterion was the difference in antidepressant response between groups during sham phase as well as long-term effect of unblended DB stimulation.

Results: A significant difference in antidepressant effect was found in month two after stimulation onset between groups. Surprisingly, this difference was not found in the first month, because both groups responded significantly after stimulation onset; in group B, this effect was time-limited (three weeks). A significant antidepressant effect at 12 months of DBS was observed on the group level. Main side effect was strabism at higher stimulation currents. No change in cognition was identified.

Conclusions: This study demonstrates a significant difference in efficacy of sham and real stimulation in a larger sample. This confirms previous efficacy data from our group (1) in an unblinded study in a smaller sample. For few weeks, some of the sham-stimulated patients showed a significant response. This can either be explained by a transient placebo effect but likely presents a lesioning effect such as described in DBS for movement disorders.

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#8865

Deep Brain Stimulation to the Superolateral Medial Forebrain Bundle for Severe, Chronic Treatment-Resistant Depression – Long-Term Outcomes

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Keywords: Major depression, Deep brain stimulation, slMFB, Outcome, Long term.

Background: Several targets for deep brain stimulation (DBS) have proven antidepressant efficacy for the treatment of otherwise treatment-resistant depression (TRD): a reduction of symptom severity of 50% in about 50% of patients could be demonstrated. The supero-lateral branch of the medial forebrain bundle (slMFB) was hypothesized to be a more efficacious target and rapid antidepressant effects were observed in seven patients. Long-term clinical data including quality of life, side effects and cognition covering four years are presented in order to evaluate clinical efficacy.

Methods: Eight patients suffering from TRD were treated with DBS bilaterally to the slMFB. Primary outcome criterion was a 50% reduction in depression severity at 12 months compared to baseline. Secondary measures were general functioning, quality of life, safety and cognition as assessed for up to for 4 years.

Results: Six of eight patients were responders at 12 months (75%), among them, four patients were remitters (50%). Long-term results revealed a stable antidepressant effect for up to four years. Clinical efficacy was also reflected in a substantial improvement of the global assessment of functioning. Main side effect was strabism at higher stimulation currents. No change in cognition was identified. Timeline analysis revealed a significant reduction in depression for 7/8 patients in all months (87.5%).

Conclusions: Long-term results of DBS to the slMFB for TRD suggest a rapid and sustained antidepressant effect; timeline analysis may be a more meaningful approach in assessing long-term outcome in TRD clinical studies. In order to validate the antidepressant effect of slMFB-DBS, the inclusion of a sham phase in further studies is needed.

Radiosurgery

#8415

Gamma Knife Radiosurgery for Secondary Trigeminal Neuralgia Associated with Benign Tumors and the Retrogasserian Trigeminal Nerve Target

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Keywords: Gamma-knife radiosurgery, Meningioma, Retrogasserian target, Secondary trigeminal neuralgia, Tumor-related trigeminal neuralgia.

Objective: To investigate gamma knife radiosurgery (GKS) for benign tumor-associated secondary trigeminal neuralgia (TN).

Methods: From 2006 to 2015, 21 patients with secondary TN from meningioma were treated by GKS. The mean age of patients was 56.5 ± 12.2 years. The 50% isodose was 12.5 ± 1.1 Gy for the first GKS for meningioma. Retrogasserian targeting of the trigeminal nerve at 90 Gy with a 4-mm collimator was used for the second GKS.

Results: The delay from the onset of pain until GKS was 1.9 ± 1.9 years. The meningiomas were located in the cisternal space in 13 patients (56.5%) and involved the skull base in 8 patients (43.5%). The mean follow-up duration was 3.7 ± 2.7 years. The pain control outcomes were Barrow Neurological Institute pain scores (BNI) of I–III in 15 patients (71%). In six (29%) BNI IV patients, we performed a second GKS that targeted the trigeminal nerve resulting in a BNI of II–III. The tumor size did not increase in any patient and decreased >10% in 12 (80%) of the 15 patients who were followed for at least 1 year. Trigeminal nerve visibility may improve after tumor shrinkage. Retrogasserian targets could be used even with invisible trigeminal nerves using Meckel's cave as an anatomical marker.

Conclusions: We have shown the reproducible feasibility of a two-session GKS procedure using higher radiation doses: the first to treat the tumor and the second to treat the trigeminal nerves using retrogasserian targeting.

#8515

Raising Quality through Implementation of a Robust External Credentialing Program for SRS and SBRT: Novalis Certification Experience

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Keywords: Stereotactic radiosurgery, Stereotactic body radiotherapy, Quality, Patient outcomes.

Introduction: External reviews of specialized radiation modalities such as SRS and SBRT has been recommended by various organizations including ASTRO to insure the highest quality of patient care. Until recently, there existed no international program that met all the requirements of peer reviewed analysis and recommendations designed to accomplish this. The Novalis Certified program was created to fill this need. This study reports on the early experience and success of the Novalis certification program.

Process: The program was conceived and developed through an iterative process involving identified experts in medical physics, radiation oncology and neurosurgery. The result was a comprehensive standards document, based on national and international standards with detailed requirements in program structure and clinical application, personnel, training, technology, and quality management. The voluntary credentialing process includes an institution-generated self-study and extensive off-site document review followed by a one-day, onsite audit. Reviewers generate a descriptive report, which is reviewed by the multidisciplinary expert panel. Outcomes of the review may include mandatory requirements and optional recommendations.

Results: A total of 125 institutions have enrolled in the Novalis certification program. To date, 17 have received Novalis Certification, including 3 in the US, 7 in Europe, and 6 in Asia/Pacific, 1 in Latin America. The initial reviews generated 9 required actions, which were all addressed within three months of the onsite review. In addition, 84 specific recommendations ranging from programmatic to technical in nature were identified. Survey of reviewed Institutions indicates the credentialing process addressed a critical need and was highly valuable to the institution.

Conclusions: Novalis Certification is a unique peer review program assessing safety and quality in SRS and SBRT, based on international standards, that recognizes high caliber practice. The approach is capable of highlighting outstanding requirements and providing recommendations to enhance both new and established programs. Independent credentialing programs can potentially have a significant impact in ensuring quality and safety in specialized radiotherapy programs.

#8813

Brain Metastases Treated with Frameless Radiosurgery

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Keywords: Brain metastases, Frameless radiosugery.

Introduction: Frameless radiosurgery has become a technique increasingly used for the treatment of brain metastases. A non-invasive system mask with Image Guided Radiation Therapy (IGRT) is a very attractive and comfortable alternative (Elekta ® system).

Objective: We evaluate our clinical results in brain metastases treated with frameless radiosurgery plus IGRT.

Patients and Methods: In ONCOSUR-Granada, between August 2010 and April 2016, we have treated 40 patients (50% male) with 131 brain metastases (1–11) and a mean age of 58.68 years (33–83). We have performed a total of 62 treatments. Our PTV margin was 2–3 mm. We have evaluated the clinical and therapeutic data.

Results: Primary tumors were 17 lung, 10 breast, 5 melanomas, 2 kidneys, 1 cervix, 1 esophagus, 1 rectum, 1 ovary, 1 unknown primary, and 1 bladder. Only 16 patients were also treated with whole brain radiotherapy (WBRT). Radiation therapy techniques used were: 41 Volume Modulated Arc Therapy (VMAT); 21 Intensity Modulated Radiation Therapy Step-and-Shoot (IMRT SS). The hypofractionation schemes used were: 6 x 6 Gy fractions (8 cases) and 10 Gy x 3 fractions (16 cases). All patients received 2–3 weekly fractions. In the literature the positioning accuracy was between 1 to 4 mm for frameless stereotactic systems. In our series, the variation in repositioning with IGRT was: X = 0.24 mm (0.01–0.65); Y = 0.23 mm (0.06–0.66); and Z = 0.23 mm (0.01–0.45). No severe side effects were detected. With a mean follow-up of 11.1 months (1–102), 7 patients are alive, 32 died (19 of them without WBRT). Our local control was 60% (treated patients have an average of 3.3 lesions). The causes of death were: brain progression in 16 patients; lung progression in 8 patients; liver progression in 2 patients; unknown reason in 4 patients and general deterioration in 3 patients.

Conclusions: Frameless radiosurgery is effective for local control and a comfortable treatment in the treatment of brain metastases. The noninvasive mask system plus IGRT is associated with a highly accurate repositioning.

#8814

Stereotactic Body Radiotherapy (SBRT) in Spine Metastases

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Keywords: SBRT, Spine, Metastases.

Introduction: Stereotactic Body Radiotherapy (SBRT) has become a technique increasingly used for the treatment of spine metastases versus conventional radiotherapy. The objective of this technique is to improve local control, relieve symptoms quickly, restore neurological status, prevent spine instability and the reirradiation.

Objective: To evaluate our clinical outcomes in selected spine metastases patients (KPS >70% and three vertebral locations but no more than two consecutive lesions) treated with LINAC SBRT plus Image Guided Radiotherapy (IGRT) (Elekta Synergy®).

Patients and Methods: In ONCOSUR-Granada-Cordoba, between August 2010 and April 2016, we have treated 15 patients (8 women and 7 men) with 24 locations (1–3 metastases) and a mean age of 64 years (42–82). The protocol includes a 2-mm CT with oral contrast to the esophagus and MR study of 2 mm. The bone has been outlined in T2 (6 mm above and below the afected vertebral body). Volumes have been identified following the criteria of the International Spine Radiosurgery Consortium (ISRC). We have evaluated the clinical and therapeutic data.

Results: Primary tumors were: breast (4), lung (2), kidney (2), colon (2), sarcoma (2), prostate (2), and unknown primary (1).

Radiation therapy techniques used were: 22 locations with Volumetric Modulated Arc Therapy (VMAT); 2 Intensity Modulated Radiation Therapy Step-and-Shoot (IMRT SS). The hypofractionated schemes used were: 9 Gy x 3 fractions (15 locations), 8 Gy x 3 fractions (2); 6 Gy x 5 fractions (2), 5 Gy x 8 fractions (1) and 6 Gy x 4 fractions (2). All patients received sessions on alternate days. No acute side effects (mielitis or spine fractures) were detected. With a median follow-up of 11 months (4–28). Two patients are still under treatment. Nine patients are alive (60%), 4 with over 1 year survival and two of them free of disease.

Conclusions: The spine SBRT is effective for local control and a safe and comfortable treatment of spine metastases. SBRT must be promoted for selected patients with oligometastatic disease, tumors resistant to the standard fractionations and higher probability of survival at one year (breast and prostate).

Spasticity

#8862

Selective Monitorized Neurectomy in Combination with Electrical Peroneal Nerve Stimulation for Treatmnent of Drop Foot Syndrome and Complicated Spasticity in Stroke Patinets

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Keywords: Neurectomy, Drop foot, Stroke, Spasticity.

Introduction: Drop foot syndrome (DFS) and spasticity are common proiblems in postsroke patients with a severe impact on quality of life. For the first problem, electrical stimulation of the peroneal nerve has been etsablished as effective treatment within the recent years. DFS is often complicated by spasticity blocking the adjacent or more distant articulations, such as the knee, the hip, or even in the upper extremity. This can limit the effectivity of peroneal stimulation and may create complex walking difficulties.

Methods: Within a series of 30 patients with an implanted peroneal stimulator (Actigait, Otto Bock(R)), we identified 5 patients with complicating severe spasticity (before the Actigait implantation). Those were identified by a careful computer assisted gait analysis. Afterwards, selective blockades of the nerves were performed as a test. In all 5 patients, there was a temporary significant improvement of gait in this testing phase. After having identified the relevant muscles by these tests, we performed a combined treatment by microsurgical selective monitoriezed neurectomy (cutting only motoric branches of the involved nerves). During the opration, the treating neurologist from the Rehazenter (R) was present in the OR to identify intraoperatively by EMG the responsible nerve fibres. The neurectomy was performed under microsurgical conditions over at least 1 cm lenght per nerve. All patients got neurectomies in the lower and one additionally in the upper extremity.

Results: For all patients, the relevant motoric nerve branches could be identified intraoperatively. There was no complication due to the operative procedures (neurectomy and peroneal stimulation). Especially, due to the restriction to purely motoric branches, there was no postprocedural neuropathic pain. With follow-up times between 3 months and 2.5 years, all patients have a significant benefit of gait due to this combined treatment. During the presentation, we will provide videos pre-, post- and also intraoperatively.

Discussion: To our knowledge, this is the 1st series with combined selective microsurgical neurectomy and peroneal nerve stimulation. According to our experience, yet limited by only 5 patients, that far, this is a sfe and effective treatment possibility for patients with central drop foot syndromne and complex spasticity.

#8898

Stereotactic Cerebellar Stimulation – Past-Present-Future

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Keywords: Deep cerebellar stimulation, Cerebral palsy, Vegetative state.

Deep cerebellar stimulation has been applied for symptomatic treatment of spasticity, dyskinesias in 45 patients suffering from cerebral palsy and 4 comatous patients after severe brain injury. Selection of the target area, parameters of the stimulation, its clinical effectiveness will be discused.

Stereotactic and Functional Neurosurgery

Brain Machine Interface and Imaging

#8496

Fiber Tractography and Brain Atlas Integration in Stereotactic Planning: Improving Interactivity with Multithreaded and CUDA-Based Solutions

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Keywords: Stereotactic planning, Interactive tractography, atlas fusion, CUDA-multithreaded programming.

In order to support surgical planning with computationally intense tractography analyis and brain atlas fusion, it is important to find a smooth integration with multithreaded or GPU-based approaches. The available open source libraries offer solutions but the parameter intialization, intermediate data exchange, interactive visualization of results are related to surgical planning steps and remain challenging.

Fiber tractography is initiated from our Vister3D surgical planning software by command scripts calling MRtrix library functions (http://jdtournier.github.io/mrtrix-0.2/) suitable to perform multithreaded diffusion-weighted MRI white matter tractography. Selection of anatomical MR sequence initiates automatic parsing of diagnostic files to find DWI data of patient. Spherical ROIs are defined in 3D using orthographic views of anatomical sequence. Locations are mapped from radiologic (LPS) to neurologic (RAS) patient space and transformed to the scanner reference. From there the space of DWI data can be reached and streamline or probabilistic tractography are executed. The resulted fiber models transformed back to the imaging space representing patient anatomy and displayed in the surgical planning views. The fiber models are visualized during frame based stereotactic planning and also during frameless navigation in different real-time resampling modes. The tractography analysis is supported by multiply ROI selection which can involve not only the 'seed' type ROI but also 'exclude' and 'include' type ROIs. The computations are very fast, streamline computations with single seed ROI run less than one minute and probabilistic ones with the same ROI usually less than 10 minutes.

Brain atlas fusion is added to Vister3D planning in interactive way by using NVIDIA CUDA-based fast, nonlinear 3D image fusion algorithm (https://sourceforge.net/projects/ezys/). The registration is limited for subvolume, position and size of it are initiated in atlas volume according to user-selected group of atlas seeds. The size of atlas subvolume and target subvolume in patient reference is kept identical but can be modified from patient volume. The center of subvolume in atlas domain is left fixed in contrast to the subvolume in patient domain where it can be relocated. This positioning can be used to find the best initial overlap for optimization. The planning software creates archives for subvolumes in atlas and patient MR domains together with parameters needed for actual registration. Weight distributions in 3D can be defined for atlas and reference volumes to amplify effects of some parts of image in computations. The fusion aligns atlas based subvolume to patient subvolume usually in few seconds. The displacement field is used to deform seeds into the patient reference. The seed voxel distribution is smoothed with 3x3x3 Gaussian filtering method in reference volume and transformed to different planning views with CT or MR modalities.

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#8887

Diffusion Tensor Imaging Tractography Assisted Direct Targeting of the Cerebello-Thalamo-Cortical Network for Deep Brain Stimulation in Tremor – Surgical Strategy and Intra-Operative Effects

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Keywords: DRT, Tremor, Tractography, Fiber tracking, DTI.

Background: Deep brain stimulation alleviates tremor of various origin. Several regions like the ventralis intermediate nucleus of thalamus, the caudal zona incerta and the posterior subthalamic region are generally targeted. Previous work with fiber tractography has shown the involvement of the cerebello-thalamo-cortical network in tremor control (1–3).

Objective: We report the intraoperative results of an uncontrolled case series of tremor patients that underwent DTI FT assisted DBS of the dentato-rubro-thalamic tract (DRT).

Methods: A total of n = 27 patients (62.7 ± 14.4 years, 13 female) were enrolled (Essential Tremor (13), Encephalitis disseminate (6), Parkinson's tremor (4) and myoclonic tremor in myoclo-

nus dystonia (3)). A total of 48 DBS electrodes where implanted. Preoperatively, a clinical 32-direction (Philips, Intera 3T scanner, Best Netherlands) or 67 direction (Siemens, TRIO Tim, Erlangen, Germany) diffusion tensor magnetic resonance imaging sequence was acquired together with high-resolution anatomical T1W and T2W sequences. The dentato-rubro-thalamic tract (DRT) was individually tracked as described before (1–4). The targeting procedure has previously been described in detail (3). Individual asymmetries of the DRT were taken into account and trajectories adjusted in order to reach the DRT in the subthalamic region at its full extent. Stereotactic surgery was performed with a Leksell G-Frame (Elekta, Sweden) with the patients awake. Test electrodes were lowered into the target region via Microdrive (FHC, USA) in 2 mm steps typically starting 10 mm above target. Intraoperative tremor reduction graded on a 4 point scale (0 = no tremor reduction, 3 = full tremor control) and recorded together with the current amplitudes necessary (0.5–4 mA, 100–150 Hz, 100 us, Cosman Lesion generator, USA). The amplitude needed to reduce tremor was expressed as TiCR (tremor improvement to current ratio = Ti/I[mA].

Results: A total of 46 out of 48 finally implanted DBS electrodes were positioned on the planned trajectory (96%) and 52 trajectories were tested in 48 electrode placements (1.02 trajectories tested per implanted DBS electrode). Six DRT trajectories were planned according to a visualized asymmetry and indeed proved sufficient during stimulation thus compensating for individual anatomical variability. Electrodes were implanted on the first pass. TiCR values increase significantly in proximity to the DRT. TiCR values close to the DRT are larger than values close to the ACPC-defined Vim-region (thalamic level).

Conclusion: Based on previous work (1–3) we used DTI FT to individually target the DRT (4). The DRT is an individually targetable fiber structure that shows tremor reducing effects when modulated with the DBS technology (3). Tractography techniques can be used to directly visualize the DRT and therefore optimize target definition in individual patients. This might reduce invasiveness of the DBS approach and in the future might allow for DBS surgery under general anesthesia. We have started to use this targeting technology in two prospective trials (www.clinicaltrials.gov; Deep braIn Stimulation for Tremor TractographIC Versus Traditional, NCT02491554; One Pass thalamIc aNd subthalamIc stimulation, NCT02288468) (4) and furthermore feel confident to use it in daily practice.

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Epilepsy

#7988

SEEG Guided Radiofrequency-Thermocoagulation: A Potential Method for Pre-Resection Minimal Invasive Therapy

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Keywords: Stereo EEG electrodes, Radiofrequency.

Introduction: Minimally invasive techniques in epilepsy surgery offer many advantages to conventional surgery including addressability, cost reductions and a decrease in primary and secondary morbidity. (Quigg and Hardy, 2014) Radiofrequency thermocoagulation (RFTC) on the same depth electrodes used for diagnosis has been demonstrated to be safe and moderately effective (Guenot 2004, 2008, 2011; Catenoix 2008, 2015) although a limited number of centers have reported their series. We are presenting the initial results obtained in our center.

Methods: eight patients received RFTC treatment at the end of their SEEG procedure from Jan. 2015 to April 2016. Lesions were produced between 2 contiguous contacts on depth electrodes (Dixi, Becancon, FR) implanted with custom (FHC Inc, Maine, USA) and standard (Leksell, Elekta, Stockholm, SW) stereotactic frames allowing reaching most difficult targets. A 50-V, 120-mA current was applied for 10 to 40 seconds to reach an estimated temperature of 78–82 C. Tissue impedance was monitored throughout the procedure. Contacts in the cortex showing low voltage fast activity or spike and wave activity at seizure onset were targeted. Prior physiologic responses obtained at direct electrical stimulation (DES) were an exclusion criteria. Lesions morphology was estimated at 3 months with post-procedure MRI.

Results: 2 to 10 contact pairs were coagulated per procedure (6 patients had frontal epilepsy, 1 occipital and 1 opercular). 6 were MRI negative cases – classically not viewed as candidates for RFCT, while 2 showed a malformation of cortical development. Median follow-up was 6 months (range 1–15). 3 (37%) are seizure free (Engel I A), 4 (50%) experienced a significant improvement in either seizure frequency or seizure duration (Engel III) 2 of which after an initial seizure free period, while 1 (13%) obtained no benefit. No acute or long-term complications were registered.

Conclusions: Our early experience, confirms the technique's safety profile and efficiency, even in a difficult non-lesional population.

#8431

Methodology, Outcome, Safety and in vivo Accuracy in Traditional Frame-Based Stereoelectroencephalography

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Keywords: Stereoelectroencephalography, Stereotaxy, In vivo accuracy, Complications, Epilepsy surgery.

Background: Stereoelectroencephalography (SEEG) can be used for the localization of the epileptogenic zone (EZ) in drug-resistant epilepsy. In vivo accuracy of SEEG electrode positioning is of paramount importance, since higher accuracy may lead to improved EZ localization, more precise resective surgery, potential better seizure outcome and reduction of neurological complications.

Objective: To describe the start and first experience of the SEEG technique in our epilepsy center, to illustrate the surgical methodology, to evaluate in vivo application accuracy and to consider the diagnostic effect of SEEG-implantations.

Methods: All patients who underwent SEEG implantations between September 2008 and April 2016 have been analyzed. After fusion of pre- and postoperative imaging, planned electrode trajectories were compared with post-implantation trajectories. Quantitative analysis of deviation using Euclidean distance and directional errors was performed. Explanatory variables for electrode accuracy were analyzed using linear regression modelling. Additionally, surgical methodology, procedure-related complications and diagnostic outcome were reported.

Results: Seventy-six implantations were performed in 71 patients and a total of 902 electrodes were implanted. Median entry and target point deviation (calculated in 866 trajectories) were 1.54 mm (interquartile range (IQR) 0.92–2.28 mm) and 2.93 mm (IQR 1.98–4.20 mm), respectively. Factors that predicted entry point accuracy were electrode orientation (orthogonal/oblique), temporal implantation, planning scan modality (CT/MRI), skin-skull distance and skull angle. Target point accuracy could be predicted by entry point accuracy and all variables related to it, electrode deviation and skull thickness. Major complication rate (persistent neurological deficits or necessity of surgical re-intervention) was 2.7% (n = 2).

Conclusions: SEEG is a precise method for the presurgical evaluation of drug-resistant epilepsy, as demonstrated by the high accuracy of traditional frame-based implantation methodology and the good diagnostic yield. We demonstrated that entry and target point localization errors can be predicted by linear regression models, which can aid in identification of high-risk electrode trajectories and further enhancement of SEEG accuracy.

#8476

Subcortical Band Heterotopia. Results from Two Cases Submitted to Anterior Nuclei of the Thalamus Stimulation

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Keywords: Epilepsy, Deep brain stimulation, Migration disorder, Subcortical band heterotopia.

Introduction: Patients with a neuronal migration disordered characterized by subcortical band heterotopia are prone to develop refractory epilepsy. Some attempts have been made to treat this condition surgically with Stereo-EEG and focal resections with discouraging results. In our series of deep brain stimulation of anterior nuclei of the thalamus (DBS-ANT), from 12 patients, 2 were due to this development disorder.

Case Study: Seizure outcome was reviewed now at 12 and 18 months en patient 1 and 2. Both patients showed a greater than 50% decrease in seizure frequency and an increase in seizure free time. After surgery they both had a transient depressive syndrome that responded to anti-depressive medication.

Discussion: Deep brain stimulation of ANT has shown a good seizure outcome in these two cases. We propose that this procedure could be considered in the treatment of patients with subcortical band heterotopia with refractory epilepsy. The etiology of depression is probably multifactorial but might be a transient adverse event of DBS-ANT.

#8528

Subfrontal Selective Amygdala-Hippocampectomy via a Supraorbital Craniotomy: Long-Term Follow-Up of Two Patients

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Keywords: Selective amygdala-hippocampectomy, Supraorbital craniotomy.

Objective: To describe the technique, results and limitations of the supraorbital approach for amygdala-hippocampectomy (AHE).

Methods: Two patients underwent presurgical epilepsy diagnostics and were rated as surgical candidates, in order to cure pharmacoresistent mesial temporal lobe epilepsy. Via supraorbital craniotomy and subfrontal route microsurgical selective AHE was performed, using a neuronavigation system.

Results: The surgeries were conducted without difficulties. Solely the depth of the intracranial space limited the dorsal extent of the hippocampal resection. The postoperative course was complicated in one case by a thalamic infarction that led to a transient hemiparesis and impairment of fine motor skills. Both patients remained seizure free over more than five years. The right handed patient with the left sided temporal lobe epilepsy showed presurgically impaired verbal learning and memory. The left handed subject with right sided temporal lobe epilepsy also had preresective short and long term verbal memory disturbances. Neuropsychological follow-up revealed no relevant changes in performance of the two patients.

Conclusion: The supraorbital/subfrontal approach is feasible and effective in performing selective AHE in drug resistant mesial temporal lobe epilepsy. The technique is sophisticated and need appropriate experience.

#8558

Invasive Intracranial Monitoring and Surgical Resections in Medially Refractory Epilepsy: Outcomes and Complications

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Keywords: Invasive intracranial monitoring, Refractory epilepsy, Surgical outcomes.

Objectives: To evaluate the epileptogenic zone in patients with medically refractory epilepsy referred to the epilepsy surgery programme with invasive intracranial monitoring and report our experience and subsequent surgical outcomes.

Design: Retrospective Review.

Subjects: 72 consecutive patients (29 male, 43 female; age range 14–60 years) who underwent invasive monitoring procedures (depth electrodes, subdural grids and strips) from March 2008 to March 2015.

Methods: Patients were identified from a prospective database. Epileptogenic zone identification, seizure semiology, subsequent surgery performed, complications and postoperative Engel scores were analysed.

Results: Over 116 months, 72 patients underwent 74 invasive monitoring procedures. Epilepsy syndromes included 51 patients with temporal lobe epilepsy, 20 patients with frontal lobe epilepsy and 3 patients with parietal lobe epilepsy. The epileptogenic zone was identified in 54 (73%) recordings (39 temporal onset, 12 frontal onset and 3 parietal onset). 14 patients had bilateral seizure onset, 4 had multifocal onset and 2 patients had no seizures recorded. Complications were two intracranial haematomas (2.7%), one retained metal lead contact (1.4%) and one localised temporal lobe oedema (1.4%).

51 patients (71%) were then deemed to be suitable for surgical resections. Of these, 36 patients underwent surgery (24 temporal, 10 frontal and 2 parietal resections), 7 are awating surgery, 5 declined and 3 were not suitable due to medical co-morbidites. Awake resections were performed in 6 left temporal and 3 left frontal resections. The most common surgical pathology was cortical dysplasia (52%). Median postoperative period was 35 months. Postoperative Engel scores of class 1 and 2 were 33% in the temporal resection group and 60% in the frontal resection group (overall 40%). Complications included 3 patients with mood changes (12%) and 1 patient each (4%) with thromboembolism, contralateral haemorrhage, transient nominal dysphasis and Stven Johnson syndrome from a subdural empyema.

Conclusion: Invasive monitoring performed as part of epilepsy surgery workup is safe and effective in localising the epileptogenic zone in patients with medically refractory epilepsy. In carefully selected patients, subsuquent surgical resections can result in satisfactory postoperative seizure control.

#8572

Deep Brain Stimulation (DBS) for Medically Refractory Epilepsy: Single Center Experience and Clinical Outcomes

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Keywords: Deep brain stimulation, Refractory epilepsy, Anterior nucleus of thalamus.

Background: Deep brain stimulation (DBS) is a promising neuromodulation therapy for patients with medically refractory epilepsy not suitable for surgical resection. The Stimulation of the

Anterior Nucleus of the Thalamus for Epilepsy (SANTE) trial has demonstrated a reduction in seizures which is sustained in the long-term [1, 2].

Methods: Eight patients (7 female, 1 male; age range 21–41 years) underwent bilateral DBS insertion from July 2012 until January 2014. Target selection was the anterior nucleus of the thalamus in 6 patients and centromedian nucleus of the thalamus in 2 patients. Preoperative evaluation consisted of electroencephalogram (EEG), video EEG, magnetic resonance imaging (MRI), neuropsychological evaluation, Liverpool seizure severity scale and Quality of Life in Epilepsy (QOLIE). Mean follow up period was 36 months.

Results: Seven patients had complex partial seizures with secondary generalization and one patient had juvenile myoclonic epilepsy Two patients had previous vagal nerve stimulator (VNS) insertion, 1 patient had a left temporal lobectomy and one further patient had previous limited left temporal lobe resection for dysembyonic neuroepithelial tumour (DNET) and VNS insertion. At follow up, 3 patients (37.5%) had more than 50% reduction in seizure frequency, 2 patients (25%) had around 50% reduction in seizure frequency, in 2 patients (25%) seizure frequency was unchanged and one patients' seizure pattern changed to drop attacks only. One patient had the DBS system removed at 27 months due to lack of efficacy. Postoperative neuropsychological outcomes were performed in 5 patients and this demonstrates improvement in mood and QOLIE in 3 patients (37.5%) and no significant change from baseline in 2 patients (25%). There were no postoperative complications or adverse device effects in the follow up period.

Conclusion: This small series replicates the results of SANTE trial providing further data in support of DBS stimulation being an efficacious and safe treatment for patients with medically refractory partial and secondarily generalized epilepsy.

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#8613

Integration of Multimodal Diagnostic Studies (MRI, fMRI, DTI, EEG) and Visualization of the Result to Aid the Planning of Epilepsy Surgeries

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Keywords: Epilepsy surgery, MRI, EEG, Integration.

Introduction and Aim: In order to investigate and map the precise epileptic mechanism (network) and seizure onset zone during the planning of epilepsy surgery we use more and more complex imaging and electrophysiological studies. The analysis and evaluation of the ever growing datasets needs such a complex platform which can integrate the spatial information derived from the preoperative structural and functional imaging data with the electrophysiological data coming from the implanted intracranial electrodes.

Materials and Methods: With the development of a custom made Matlab based software we can co-register preoperative structural and functional images with the postimplantation structural images containing the implanted electrodes. We created a special interface to combine imaging data and electrophysiological data to integrate the electrophysiological maps (interictal discharges, seizure onset zone, high frequency oscillations, cortical electrical stimulation, cortico-cortical evoked potentials) in to the same space where the imaging data is presented.

Results: The coregistration of the different structural and functional (fMRI, DTI) 3D imaging data is already possible using open source softwares. The coregistered images are automatically transformed to the patients own MRI space and to standard space as well where using the postimplantation CT images we can determine the exact position of the electrodes. Using our custom made software now we can visualize the most important electrophysiological and stimulation data on the patient's individual anatomy using the location of the electrodes as connection between different modalities.

Conclusions: The presented method allows the precise and automated coregistration of different imaging modalities and electrophysiological data. The integration of the complex electrophysiological data and maps into the same space allows more precise decision making in complex epilepsy surgical cases and allows more precise demarcation of the epileptogenic zone. The most difficult challange to solve in today's epilepsy surgery is to integrate all the information collected in one patient to create the best surgical plan and to resultong in the best epileptological outcome possible.

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#8806

Stereo-Electroencephalography Using Magnetic Resonance Angiography for Avascular Trajectory Planning

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Keywords: Drug resistant epilepsy, Epilepsy surgery, Magnetic resonance angiography, SEEG.

Background: Stereo-electroencephalography (SEEG) requires high quality angiographic study because avascular trajectory planning is a prerequisite for the safety of this procedure. Some epilepsy surgery groups have started to use computed tomography angiography (CTA) and magnetic resonance T1-weighted sequence with contrast enhancement (CE T1). To the best of our knowledge there are no reports of avascular trajectory planning of SEEG based on magnetic resonance angiography (MRA).

Objective: The goal of our study was to assess the quality and safety of MRA for avascular trajectory planning of SEEG.

Methods: Thirty-six SEEG explorations for drug-resistant focal epilepsy have been performed from January 2013 to December 2015 in the Epilepsy Surgery Center in Sofia. MRI included MRA with modified contrast enhanced magnetic resonance venography (MRV) protocol with short acquisition delay allowing simultaneous arterial and venous visualization. Our criteria for satisfactory MRA were visualization of at least first-order branches of the angular artery, paracentral and calcarine artery and third-order tributaries of superficial Sylvian vein, vein of Labbe and vein of Trolard.

Results: Thirty-four patients underwent thirty-six SEEG explorations with 369 electrodes carrying 4321 contacts. Contrast enhanced MRA using MRVprotocol was judged satisfactory for SEEG planning in all explorations. Postoperative complications were not observed in our series of 36 SEEG explorations.

Conclusions: MRA using MRV protocol may be applied for avascular trajectory planning during SEEG procedures and appears to have satisfactory safety profile. This technique provides simultaneous visualisation of cortical arteries and veins without need of additional radiation exposure or intra-arterial catheter placement.

Experimental

#8570

A Co-Manipulation Robotic System for Brain Biopsies

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Keywords: Robotic brain biopsy, Light weight robotics, Image registration.

Brain diseases affect a substantial amount of people worldwide, and brain surgery is in many cases the most efficient, but complex, therapeutic procedure to treat them. In most brain diseases, the first procedure to be performed is a brain biopsy in order to identify the type of disease.

One of the most relevant problems in brain biopsies is the ability of the physicians to execute what was planned in the pre-operative stage. In other words, once is defined a target to biopsy in the brain and the desired trajectory of the biopsy needle is planned, it is the skill of the surgeons that will assure that the procedure will be correctly performed. In many cases, the skill of the surgeons is limited by the equipment used.

The evolution of robotics, mainly in the field of human-machine interaction, has provided more precise and less invasive procedures, allowing to reduce human errors, and to overcome certain limitations of the conventional brain surgeries. Also, the evolution of robotic positioners allowed the surgeons to be focused on the surgery itself and not on the equipment.

In this project, a robotic solution involving the KUKA LWR 4+ and the Polaris Spectra optical tracking system has been implemented, in order to perform brain surgeries requiring precise targeting of structures within the brain. The robot's positioning task is performed by a co-manipulation setup between the surgeon and the robot, through a virtual impedance environment. Unlike the typical scenario of industrial robotic arms, in a co-manipulation scenario there is a human-robot interaction. In this case, the surgeon is in the robot's workspace. The robot will guide the surgeon throughout a predetermined path, resulting in an increase of the surgeon capabilities by increasing his precision and accuracy.

Two simulated brain biopsies were performed using a phantom specifically designed for the purpose. One biopsy was performed at Hospital Santa Maria in Lisbon, following the current medical procedures and using the clinical neuronavigation instrumentation. The other was performed at the Surgical Robotics Lab at Instituto Superior Técnico, using the developed neuronavigation robotic system.

The simulated brain biopsy performed at Hospital Santa Maria followed the typical steps of the current medical procedure using the clinical neuronavigation instrumentation. In the pre-operative stage, a CT-scan and a MRI of the phantom were acquired. Based on the MRI, the surgeon planned the biopsy by selecting the target points and the respective entry points, therefore selecting the desired trajectories. Afterwards, already in the surgery room, the neu-

ronavigation instrumentation is prepared. In this case study, the surgeon performed the phantom-to-medical image registration using a StealthStation Treon® of Medtronic® and fusing the images from the MRI with the CT-scan. Once the registration was concluded and the surgeon verified its quality, the biopsies were performed. With the needle in the reached targets, its position and orientation was acquired by the Polaris Spectra, expressed on the reference frame attached to the phantom.

The simulated brain biopsy performed at Surgical Robotics Lab followed a different pre-operative procedure different from the one at the hospital. Instead of using medical images, a point cloud of the phantom acquired with the Polaris Spectra was used. Based on such point cloud, the same target points and trajectories defined as the desired ones at the hospital were used. Once the planning phase was concluded, a registration phantom-to-robotic arm was performed, to establish the target coordinates in the robotic arm's workspace. Then, the biopsies were performed following the trajectories allowed by the robotic arm. With the needle in the reached targets, its position and orientation were acquired by the Polaris Spectra, expressed on the reference frame attached to the phantom.

The targeting errors of both approaches were measured, and then compared. The errors obtained with the clinical approach, from the medical image acquisition to the biopsy execution, were 3.74 mm > 1.56 mm and 3.77°±2.23° for target position and trajectory orientation, respectively. The errors obtained with the neuronavigation robotic system were 2.46 mm > 1.04 mm and 3.61°±2.75°, for target position and trajectory orientation, respectively. The results of this project reveal that using the robotic system it is possible to obtain a 34% decrease in position error and a 4% decrease in orientation error with the robotic system.

#8571

Deep Brain Stimulation of the Central Auditory Pathway Suppresses Tinnitus in Rats

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Keywords: Tinnitus, Deep brain stimulation (DBS), Auditory pathway.

Introduction: Tinnitus can be a disabling symptom, as it can lead to insomnia, anxiety, depression and even suicide in severe cases. Currently, there is no effective standard therapy. Neuromodulation is a promising treatment modality in tinnitus, especially for chronic and severe cases. Although the exact neural substrate for tinnitus is unconfirmed, multiple animal and human imaging studies related tinnitus to hyperactivity and hypersynchrony within auditory brain structures.

Objectives: We hypothesized that high-frequency stimulation (HFS) of the central auditory pathway will influence abnormal tinnitus related neuronal activity and hereby disrupt tinnitus perception. Here, we assessed the effect of deep brain stimulation (DBS) of either the dorsal cochlear nucleus (DCN), inferior colliculus (IC) or medial geniculate body (MGB) in a rat model of chronic noise-induced tinnitus.

Materials and Methods: A within-subject design was used in order to minimize the number of animals and reduce the error variance. A total of 30 male Sprague Dawley rats were assigned to three target groups: DCN, IC and MGB and underwent bilateral DBS electrodes implantation at the start of the experiment. Tinnitus was induced by unilateral noise exposure. Hearing thresholds were determined before and after noise trauma by measurements of auditory brainstem responses. Gap-induced pre-pulse inhibition of the acoustic startle response (GPIAS) testing was used to assess presence of tinnitus during four main conditions: 1) baseline DBS off, 2) baseline DBS on, 3) post noise trauma DBS off and 4) post noise trauma DBS on. Standard stimulation was HFS and two additional stimulation paradigms were tested after tinnitus induction in all subjects of the MGB group, namely after HFS (DBS off after 30 minutes of HFS) and during low-frequency stimulation (LFS). Anxiety-related side effects of HFS were evaluated in the elevated zero maze and open field.

Results: ABR measurements demonstrated preserved hearing thresholds of the side that was protected from noise trauma. GPIAS for tinnitus assessment showed a significant chronic tinnitus development after noise-trauma at the 16 kHz and 20 kHz frequency bands. HFS did not lead to a change in gap:no-gap ratios at baseline, but caused a significant decrease of the gap:no-gap ratios of 16 kHz and 20 kHz after tinnitus induction in all targets. In the MGB group, a persistent effect on tinnitus suppression was found directly after HFS was turned off, but no effect was found of LFS on the gap:no-gap ratios of the acoustic startle response. No anxiety-related side effects were found during DBS.

Conclusion: These results suggest that neuronal hyperactivity in the auditory pathway can be normalized with HFS in different levels of the auditory pathway. Optimal stimulation parameters need to be investigated, as well as the effect of stimulation on hearing function. Clinically, compared to the DCN and IC, the MGB would be best accessible with stereotaxy and might therefore be an applicable DBS target if an invasive treatment is considered in severe and refractory tinnitus patients.

#8608

Endo Ventricular Deep Brain Stimulation of the Ventro-Median Hypothalamus as a Rescue Treatment in an Obese Patient Carrying a Heterozygous Mutation in the POMC Gene

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Keywords: Deep brain stimulation, Hypothalamus, Obesity, POMC.

We report the case of a woman, aged 37 years, suffering from early-onset obesity and uncontrolled hyperphagia, associated with partial endocrine deficiencies, complicated by major hypoventilation and uncontrolled type-2 diabetes (HbA1c = 9%, 240 IU/d of insulin). The sequencing of the POMC gene revealed a heterozygous mutation. POMC is the hormonal precursor of a potent anorexigenic neuropeptide (alpha-melanocyte stimulating hormone) acting on the melanocortin-4 receptor expressed in the ventro-median hypothalamus (VMH), which when activated leads to decrease the food intake.

Despite of a multidisciplinary medical approach, she reached the maximal weight of 185 kg (BMI: 75 kg/m²) at the time of inclusion. She was contra-indicated for gastric by-pass due to severe hyperphagia and worrying respiratory status. Her general health condition was rapidly declining, due to the aggravation of her respiratory condition (PaO2= 64 mm Hg, PaCO2= 56 mm Hg) leading to sharply reduced mobility and autonomy. Given the deterioration of her medical condition and no available efficient medical treatment, she was included in a hypothalamic deep brain stimulation protocol.

We implanted a single electrical stimulating electrode into the anterior third ventricle to stimulate the VMH bilaterally. At 6 months, she started to lose weight (–17%) and improved her quality of life. HbA1c significantly dropped in parallel to reduced insulin needs (–53%). More importantly, we observed an increase of the resting metabolic rate, measured by indirect calorimetry (2249 to 2673 kcal/d pre and post op respectively, 6 mo F.up) that reinforced the hypothesis of a direct modulation of energy balance by electrical modulation of the hypothalamus.

Movement Disorders

#8424

Characterizing the Micro-Lesion Effect Due to Intraoperative Microelectrode Recording on Motor Symptoms in Patients with Parkinson's Disease Undergoing Deep Brain Stimulation of the Subthalamic Nucleus

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Keywords: Deep brain stimulation, Subthalamic nucleus, Microelectrode recording, Iesion effect, Parkinson's disease.

Deep brain stimulation (DBS) of the subthalamic nucleus (STN) is an effective treatment in patients with Parkinson's disease (PD). The surgical approach can be with or without intraoperative microelectrode recording (MER). Centers using MER to delineate the neurophysiological boundaries of the STN, acknowledge its value. MER can be accompanied by spontaneous improvement of the Parkinsonian motor symptoms, which is known as a micro-lesion effect. While the phenomenon is well-known, its quantitative impact on motor symptoms is largely unknown. In this prospective study, we have studied the micro-lesion effect of MER in 30 patients with PD undergoing DBS of the STN. The change in the scores of tremor, rigidity, bradykinesia was collected using the Unified Parkinson's Disease Rating Scale. The preoperative medication off scores was compared to the intraoperative scores after MER. We found a significant change ($p < 0.05$) in the motor score due to a lesion effect only in the upper extremities The micro-lesion effect was more pronounced in tremor and bradykinesia when compared to rigidity. Although the micro-lesion effect was quantitatively higher in patients with a higher levodopa response rate, there was no significant correlation between these two parameters. Similarly, there was no significant relationship between the micro-lesion effect and age, disease duration, and the number of MER electrodes used. Micro-lesion effect due to MER in patients with PD has specific effects on the motor symptoms and is independent of the number of MER electrodes used.

#8452

Deep Brain Stimulation of the Globus Pallidus Internus in Patients with Chorea-Dominant Huntington's Disease

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Keywords: Deep brain stimulation, Globus pallidus, Huntington's disease, chorea.

Huntington's disease (HD) is an autosomal dominant and a progressive neurodegenerative disorder. It is caused by an increase in the number of CAG repeats in the *Huntingtin* gene. Patients suffer from cognitive, emotional and motor disorders. For patients with predominant motor symptoms, deep brain stimulation (DBS) of the globus pallidus internus (GPi) has been suggested. Patients with chorea-dominant HD were referred to our University hospital and underwent bilateral DBS of the posteroventrolateral part of the GPi with the distal electrodes in the external part of the globus pallidus. The patients had no severe cognitive or emotional dysfunctions or other major comorbidities. Here, we report on the clinical outcomes as measured with the Unified Huntington's Disease Rating Scale (UHDRS) at one-year postoperatively. Chorea improved in all patients substantially and patients, families and caregivers were satisfied by this improvement. One patient experienced a transient dysarthria. The stimulation frequency was set at 130 Hz and the contacts located in the GPi were activated. In our experience, patients with chorea-dominant HD, which form the vast minority of the HD population, with no major cognitive and emotional disturbances, are suitable candidates for chorea DBS-surgery.

#8458

Real World Clinical Outcomes Using a Novel Directional Lead from a Multicenter Registry of DBS for Parkinson's Disease

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Keywords: Deep brain stimulation, DBS, Subthalamic nucleus, STN, STN-DBS, Parkinson's disease, Directional DBS, Neurostimulation.

Introduction: Deep Brain Stimulation (DBS) has been shown to be an effective method in managing motor complications associated with moderate to severe Parkinson's disease (PD). However, individual outcomes and adverse effects following DBS can vary depending on the volume of tissue activated. Historically, DBS systems have used ring-shaped electrodes that produce stimulation fields with limited control over the shape of the field, thereby limiting the extent and shape of the volume of tissue activated. A pilot study of 7 PD subjects reported that a novel, directional DBS system, combining an eight-contact directional lead and an implantable pulse generator (IPG) capable of multiple independent current control (MICC), can feasibly accomplish directional current steering using permanently implanted electrodes, thereby enabling modulation of the adverse effect and efficiency thresholds (to facilitate enhanced individualization of neurostimulation) and in turn an increase in the therapeutic window (current difference between efficacy and adverse event threshold)[1]. In this report, we present real-world clinical outcomes of subjects implanted with a directional lead for the management of Parkinson's disease as part of a larger, on-going registry study.

Methods: The Vercise DBS Registry is a prospective, on-label, multi-center, international registry sponsored by Boston Scientific Corporation. The Vercise PC system is a CE-marked, multiple-source constant-current system with a rechargeable battery (Boston Scientific). Subjects in this specific cohort were implanted with a directional lead (Cartesia, Boston Scientific) included as part of a directional Vercise PC system for bilateral STN-DBS. Subjects will be followed up to 3, 6, 12 months and up to 3 years post-implantation where their overall improvement in quality of life and PD motor symptoms will be evaluated. Clinical endpoints will be evaluated at baseline and during study follow up that include Unified Parkinson's disease Rating Scale (UPDRS), MDS-UPDRS, Parkinson's disease Questionnaire (PDQ-39), and Global Impression of Change. Adverse events are also collected.

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Results: Subjects at several European Centers implanted with a directional lead were included in the Vercise DBS Registry. The accompanying report provides the study design, demographics, programming parameters, and other preliminary data from this directional lead cohort.

Discussion: The Vercise DBS Registry represents a comprehensive, large scale collection of real-world outcomes and includes evaluation of the safety and effectiveness of the Vercise DBS System. Data from this cohort will provide insight on the use of current steering with a directional lead as part of the directional Vercise PC system, and its implications in the treatment of patients.

Reference

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#8490

Directional Leads in DBS: A Recent Reliable Concept to Improve Follow-Up in Implanted Patients. Preliminary Experience

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Keywords: Deep brain stimulation, Current steering, Segmented electrodes.

In the last 20 years, thank' s to technological development and still ongoing innovations in features and materials of implantable devices, deep brain stimulation (DBS) has become one of the most effective, reliable and safe surgical procedure for treatment of many different movement disorders.

The clinical condition that has been better treated with such a tecnique is Parkinson' s disease. Neverthless, many other diseases today are good indication for DBS like dystonia, essential tremor and Giles de La Tourette syndrome. By now, many papers told DBS like a 'gold standard' in patients affected by dystonia or Parkinson's disease when pharmacological intake alone doesn' t work or has lots of troublesome collateral effects. Since 2010 we started to use a stereotactical frameless tecnique. We noticed a real improvement for patients in terms of comfort, tollerability and reducing pain during surgery. At the same time we obtained a very good precision in targeting, comparable to those of classical frame based surgery.

Innovations, mostly in hardware such as leads, extentions and IPG, goes on. We recently started to implant a new lead's generation named 'directional leads'. This lead has many different splitted or segmented contacts, that allows the clinicians to steer the electrical field mostly wherever they want, through nervous tissue obtaining clinical effect and far from brain area where instead they don't want to spread the current in order to avoid collateral effects.

From january to june 2016 we performed 8 bilateral implantations for Parkinson' s disease and dystonia. At the time of reglage, when collateral effects like motor evoked unwanted responses or limbic effects has been elicited, switching the 'hemi-contacts' allowed to make them disappeared without lessing the desired beneficial effect. An issue we faced with, was how to standardised in all implanted patients a rotational position of leads. As such, the clinicians can establish a number for any single contacts in order to compare results in different patients and in the single one over time as well. We also didn' t have an x-ray checking system in the Nexframe device, like basically any head-mounted and pin-fixed traditional stereotactical system has in itself. In other words, we needed a method that allowed to figure out the position of leads. We took two markers behind the ears to allineate during intraoperative x-ray checking. This brought to correct alignment of the lead's reference markers visible at the top of the whole group of contacts.

In conclusion, even though the number of patients is low, we believe that directional leads bring to excellent results in terms of shaping of stimulation. They are a powerfull tool in the hand of programmer clinicians potentially able to improve the outcome of the patients. Splitting of contacts gives the chance to get a higher number of contacts allowing the clinician to choose among many stimulation combinations. It turns out that therapeutic window is wider. Moreover, directional leads technology gives us the possibility to steer and deform the tridimensional electrical field shape. Warping and bending of electrical field, brings to a better results for patients, both lessening side effects and enhancing the positive benefits of stimulation. Our easy and reliable intraoperative tecnique is effective to correctly alineate in the same orientation the two leads of both sides.

#8495

Is It Worthwhile to Perform Deep Brain Stimulation in Primary Generalized Dystonia during the Childhood? A Bibliographic Review

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Keywords: Deep brain stimulation, Dystonia, Childhood.

Introduction: Primary Generalized Dystonia ('PGD') is an entity which causes progressive incapacity due to involuntary movements and abnormal postures. Deep Brain Stimulation ('DBS') is a salvage treatment that could be performed during the childhood, with promising results, but there is not still enough experience.

Material and Methods: A bibliographic review is performed during the interval 2005–2014, including the information related to the age of onset and age at DBS, DYT-1 status and the preoperative and postoperative Burke-Fahn-Marsden Dystonia Rating Scale ('BFMDRS') in those patients with a follow-up larger than 3 months.

In those patients with a watchfulness period larger than 12 months, the proportion of life lived with dystonia was calculated in order to perform a linear regression study comparing this data with the effectiveness of Deep Brain Stimulation, using the Burke-Fahn-Marsden scale as the dependent factor. The complications during the follow-up were also registered. The data were analysed with SPSS v21.0.

Results: 125 patients younger than 21 years old were recruited in 20 clinical studies during this period. DYT-1 mutation was observed in 71.2% of the patients, which resulted in a later onset of the disease (8.16 vs. 6.17 years, p = 0.011) and a better response to DBS in the Burke-Fahn-Marsden Dystonia Rating Scale (83% vs. 58% in motor part, p = 0.000; 78% vs. 52% in functional part, p = 0.002) 110 patients had a surveillance period larger than 12 months. In these patients it was observed a weak inverse correlation between the proportion of life ill and the 'DBS' effectiveness in both parts of BFMDRS scale, measured with the Spearman's rank correlation coefficient (–0.322 in motor part, p = 0.001; –0.302 in functional part, p = 0.012). The rate of complications was 47.9%, which is slightly worse than in adults. Hardware and infectious complications were the most frequent ones, but there were not an increase in life-threatening complications compared with adult population.

Conclusions: Deep Brain Stimulation is an effective treatment for Primary Generalized Dystonia. It must be considered when the best medical options are over, especially in DYT-1 positive patients because of their better response to this surgical technique. Those patients with shorter evolution of the illness seemed to have a better response to DBS, but further prospective studies might be performed.

#8498

Surgical Replacement of Implantable Pulse Generators in Deep Brain Stimulation: Adverse Events and Risk Factors in a Multicenter Cohort

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Keywords: Deep brain stimulation, Implantable pulse generator, Adverse events.

Background: Deep brain stimulation (DBS) is a growing treatment modality and most DBS systems require replacement of the implantable pulse generator (IPG) every few years. The literature is rather scarce regarding the potential impact of adverse events of IPG replacement on the longevity of DBS treatments.

Objectives: To investigate the incidence of adverse events, including postoperative infections, associated with IPG replacements in a multicenter cohort.

Methods: Medical records of 808 patients from one Australian and five Swedish DBS centers with a total of 1293 IPG replacements were audited. A logistic regression model was used to ascertain the influence of possible predictors on the incidence of adverse events.

Results: The overall incidence of major infections was 2.3% per procedure, 3.7% per patient and 1.7% per replaced IPG. For 28 of 30 patients this resulted in partial or complete DBS system removal. There was an increased risk of infection for males (odds ratio (OR) 3.6, $p = 0.026$), and the risk of infection increased with the number of prior IPG replacements (OR 1.6, $p < 0.005$).

Conclusions: The risk of postoperative infection with DBS IPG replacement increases with the number of previous procedures. There is a need to reduce the frequency of IPG replacements.

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#8517

Gamma Knife VIM Thalamotomy with Focus on Patient Selection, Targeting and Complications

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Keywords: Gamma Knife thalamotomy, Tremor, Parkinson's disease.

Intoduction: Gamma Knife radiosurgery is a well-known non-invasive alternative to ablative surgery and deep brain stimulation for patients with drug-resistant tremor. The modern conception of Gamma Knife thalamotomy is based on precise MRI targeting which allows one to take into account the individual anatomy of the thalamic region and to avoid complications associated with radiation damage to the internal capsule.

Methods: From January 2011 to May 2016, 55 patients with Parkinson's disease were treated with Gamma Knife 4C and Perfexion in the Radiosurgical centre (Saint Petersburg, Russia). In total, 67 radiosurgical procedures were done: 50 patients underwent a unilateral procedure, 5 patients were subjected to staged bilateral procedures, 2 patients underwent repeated radiosurgery on the same side because of the absence of effect due to incorrect targeting. The study group consisted of 41 men and 14 women with a mean age of 59 years. The procedure of Gamma Knife thalamotomy was carried out according to the standard methodology, comprehensively described by Prof. Jean Regis and others. A single 4-mm isocenter was used to deliver a maximum dose of 130 Gy to the ventral intermediate nucleus. 43 patients were subjected to clinical assessment at 3, 6 and 12 months following radiosurgery, with 23 patients undergoing neuroimaging follow-up.

Results: In total, 29 patients experienced significant improvement of tremor after Gamma Knife thalamotomy. 12 patients (55%) from our initial treatment group did not reveal a positive effect, which was later explained by incorrect targeting. Among those patients who were given treatment with more precise targeting taking into account individual anatomical features tremor relief was achieved in 80% of cases. Within this group the patients reported a complete disappearance of tremor in a median time of 5 months after radiosurgery. Repeated radiosurgery was performed in a median of two years in the case of bilateral tremor when the first procedure had a positive outcome. Complications were observed in 3 patients. One year after treatment one patient's MRI revealed intrathalamic hemorrhage on the side of the radiosurgery without any clinical manifestations; another patient suffered hemorrhagic stroke within two days after radiosurgery, due to which he underwent surgery and completely recovered thereafter. Yet another patient developed severe edema in the region of radiation exposure leading to hemiparesis. However, all three patients showed excellent tremor control. Analysis of the absence of any positive effect among a number of patients from the initial treatment group revealed that the reason lay in mistrageting and insufficiently thorough candidate selection.

Conclusion: The success of Gamma Knife thalamotomy results from correct patient selection, precise targeting accounting for anatomical differences, careful adherence to details of the radiosurgical procedure and performance of high resolution thin slice MRI. Individual radiosensitivity may be considered a reason for the absence of any positive effect, which cannot presently be predicted.

#8526

The Relative Value of Magnetic Resonance Imaging, Microelectrode Recordings and Intraoperative Test Stimulation in Final Electrode Placement during Deep Brain Stimulation Surgery of the Subthalamic Nucleus

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Keywords: Deep brain stimulation, Subthalamic nucleus, Magnetic resonance imaging, Microelectrode recordings, Test stimulation, Awake surgery.

Deep brain stimulation (DBS) of the subthalamic nucleus (STN) is the most effective surgical procedure for patients with advanced Parkinson's disease (PD). Precise targeting of the STN is paramount for maximizing therapeutic benefits while minimizing side effect. In most DBS centers, preoperative visualization of the STN on stereotactic T2-weighted magnetic resonance imaging (MRI), neurophysiological mapping of the target region through microelectrode recordings (MER) and intraoperative test stimulation in awake patients are performed to optimize STN targeting. However, it is unclear to what extent these different operative steps influence the decision where to implant the final electrode during DBS surgery.

In the current study we retrospectively analyzed the relative value of these three operative steps in final electrode placement in 76 patients with advanced PD undergoing stereotactic Leksell frame-based implantation of 147 STN electrodes. In all patients, we used 3-channel MER with the planned MRI trajectory as the central channel, with additional anterior and lateral channels at 2-mm distance from the central channel. The central channel (=planned MRI trajectory) was chosen for final electrode placement in 39% of all leads, the anterior channel in 46%, and the lateral channel in 10%. In 5%, final electrodes were implanted in another channel (medial or anteromedial). In only 12 of 71 bilaterally operated patients (17%), final electrodes were implanted bilaterally in the planned MRI trajectory. In 50% of all leads, the channel chosen for final electrode placement was the channel with the longest STN-MER signal. The reason for not choosing the planned MRI trajectory for final electrode placement was most often low threshold for lateral (internal capsule) side effects during test stimulation, followed by no or very short STN-MER signal or

medial (autonomic and oculomotor) side effects. The reason for not choosing the channel with longest STN-MER signal for final electrode placement was low threshold for lateral (internal capsule) side effects during test stimulation for almost all cases.

In conclusion, the results of the current analysis suggest that both MRI, MER and awake test stimulation all contribute to the decision where to implant the final electrode during STN DBS surgery. Their relative values should be kept in mind when considering performing STN DBS surgery without MER or under general anesthesia.

#8536

Relating Active Contact Localization in STN DBS to Long-Term Motor Symptom Outcome; Medial Border of STN as New Anatomical Reference Point

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Keywords: STN, Deep Brain Stimulation, Parkinson's disease, Red nucleus, Active contact point.

Objective: Relating active contact localization in subthalamic nucleus deep brain stimulation (STN DBS) to long-term motor symptom outcome by using midcommisural point (MCP) and medial border of STN as anatomical reference point.

Background: Good motor symptom outcome after STN DBS is assumed to require accurate implantation of DBS electrodes. However, thus far several studies found no difference in mean stereotactic coordinates of active contact relative to MCP between patient that do or do not improve well after DBS. Anatomical variance in STN size and location relative to MCP have potentially hampered such analyses. Medial border of STN may serve as a landmark less subjected to anatomical variance and could provide more insight in individual optimal point of stimulation.

Design/Methods: Stereotactic coordinates active electrode contact relative to both MCP and medial STN border were determined using preoperative stereotactic 1.5-Tesla MRI and postoperative CT. Medial STN border was determined on axial orientated MRI at the level of anterior border of the RN (Bejjani line). Resulting coordinates in X (medial-lateral), Y (anterior-posterior) and Z (dorsal-ventral) were plotted using 2D graphs. Change in off phase UPDRS motor score after 12 months of STN DBS was categorized into three groups: non-responding (less than 30%), responding (between 30 and 70%) and optimally responding (more than 70%) contralateral body-sides. Corresponding change in unilateral UPDRS motor score for individual coordinate points were subsequently integrated into the plots.

Results: A total of 50 DBS leads were evaluated in 25 patients with PD. Unilateral off phase UPDRS motor score for responding and optimally responding body-sides showed average improvement of 57% and 89%, respectively. Average change in unilateral off phase UPDRS motor score was 8% deterioration for non-responding body-sides. Active electrode contacts of optimal response were located significantly more lateral, anterior and dorsal relative to medial STN border in comparison to non-response. This 'hot spot' was situated in superolateral STN. Plots based on MCP did not show differences in contact point localization between groups.

Conclusion: Medial STN border proved to be superior compared to MCP as anatomical reference point for relating active contact localization in STN DBS to long-term motor symptom outcome. Stereotactic coordinates of stimulation points relative to medial STN border indicate an optimal area of stimulation in the nucleus. Unsatisfactory effect of DBS could be evaluated with the aid of this area and the contact point most closely situated considered for stimulation.

#8539

An Economic Evaluation of Deep Brain Stimulation for Patients with Tourette's Syndrome: An Initial Exploration

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Keywords: Economic evaluation, Tourette's Syndrome, Deep brain stimulation.

Background: Tourette's syndrome (TS) is a neuropsychiatric movement disorder. Symptoms of severe TS include involuntary tics, vocalizations and coprolalia, which can progress to affect adversely health related quality of life. Comorbidities include attention-deficit/hyperactivity disorder (ADHD), obsessive-compulsive disorder (OCD) and affective disorders. Typically, treatment may involve pharmacotherapy and supportive counselling. For a small number of patients, deep brain stimulation (DBS) is now being used to treat intractable TS. The clinical outcomes have generally been positive.

To date, no economic evaluation of treating TS with DBS has been published. A well-designed economic evaluation has become a pivotal ingredient to ensure that the necessary resources are directed towards the healthcare services, which offer the best patient outcomes. The aim of this research is to present an initial exploration of an economic evaluation of DBS to treat severe TS.

Methods: We conduct a cost utility analysis (CUA), which compares the direct medical costs reported as $US and outcomes reported as quality-adjusted life years (QALYs) of DBS with best medical treatment (BMT). Our sample consists of 17 patients who

received DBS for severe TS at St Andrews War Memorial Hospital, Brisbane, Australia from September 2008 to February 2012. The average patient age was 28. Clinical indices for (i) tic severity (Yale Global Tic Severity Score) and (ii) depression (Hamilton Depression rating Scale) and (iii) age were collected pre and post DBS. These clinical data were converted QALYs using standardized coefficients derived from a multivariate regression published by Müller-Vahl *et al* (2010) for a sample 200 German outpatients ($R^2 = 54\%$).

The direct costs for DBS, included hardware, surgical implantation, inpatient stay, neurostimulator programming and adverse events. For BMT direct costs included estimates for rehabilitation, inpatient stay, outpatient treatment, pharmaceuticals and ancillary treatments. All costs were reported in $US2016. TreeAge® software was used to estimate an Incremental Cost Effectiveness Ratio (ICER) using a Markov model, with a 10-year time horizon and 3.5% discount rate.

Results: The direct costs of DBS and BMT were estimated to be $USD 124,400 and $USD 34,180, respectively. DBS was estimated to increase health utility from 0.45 to 0.78. The ICER of DBS was estimated to be $USD 27,600 per QALY gained, which is lower than the nominal US Food and Drug Administration (FDA) approved threshold of $USD 50,000 per QALY.

Conclusions: Our initial exploration suggests DBS is a cost-effective treatment for patients with severe TS. However, our economic evaluation contains several limitations. Firstly, indirect costs were not included. Secondly, health utilities pre and post DBS were imputed from clinical data rather than measured directly. Thirdly, long-term costs and benefits are uncertain; an average age of 28 years at implant implies a further 50 years of life post DBS. The ICER was sensitive to estimates of adverse events. Finally, our results were derived from a small sample. Future research will administer a survey of healthcare costs and QALYs to an international database of TS patients treated with DBS maintained by the University of Florida, with the aim of developing a more robust economic evaluation.

#8546

Preliminary Experience with Chronic Directional DBS in the STN

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Keywords: Subthalamic nucleus, Deep brain stimulation, Directional electrode, Parkinson's disease, Volume of tissue activated.

Introduction: STN DBS has been shown to drastically improve motor symptoms of PD. However, the occurrence of disabling side effects may limit the benefit of the therapy. Computed models have suggested that directional stimulation could increase its efficacy. Intraoperative studies performed in human have shown that directional stimulation provides differents thresholds for clinical effects. In the present study, we investigate the effect of directional stimulation on beneficial and side effects, in chronically implanted patients compared to omnidirectional stimulation.

Methods: 11 bilateral STN implanted PD patients have been prospectively included in this study. In the trajectory determined after microrecording and intraoperative clinical testing, the definitive directional lead (1-3-3-1 electrode configuration, Vercise, Boston Scientific) was implantated with one electrode oriented medially, one anterolaterally and the third posterolaterally, under intraoperative fluoroscopic control. Monopolar omnidirectional stimulation was initially performed. 2–3 month after surgery, directional stimulation was assessed. The current threshold for beneficial and side effects was assessed for each of the 3 directions and compared to omnidirectional stimulation.

Results: A best direction of stimulation was observed in all patients in terms of therapeutic window. The current required to obtain a beneficial effect in the best direction showed a mean reduction of 25% compared to the omni-directional condition. The current required to achieve a sustained side effect in the worst direction was comparable to the in the omni-directional situation. The medially oriented directional electrode war found in 9/14 sides to have the highest threshold for side effects.

Conclusion: Our preliminary experience using Directional DBS in the STN performed postoperatively suggests the persistence of different thresholds for the appearance of clinical effects in directional stimulation conditions, compared to omnidirectional stimulation. Further data are needed to confirm these observations.

#8565

Long-Term Efficacy of Constant Current Deep Brain Stimulation in Essential Tremor

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Keywords: Constant current, Essential tremor, Deep brain stimulation, Constant voltage.

Objectives: The aim of this study was to evaluate the long-term efficacy and safety of the constant current devices (Libra DBS System™) produced by St. Jude's Medical in patients with essential tremor.

Design: The inclusion criteria required all the patients to have had a clinical diagnosis of essential tremor by a movement disorder neurologist, deemed suitable for DBS by a multi-disciplinary team consisting of a movement disorders neurologist, neuropsychologist, neuropsychiatrist, movement disorders neurosurgeon, and a deep brain stimulation (DBS) specialist nurse, and had a minimum of 3 years of constant current stimulation of the Vim DBS. Patients with other movement disorders were excluded.

Subject: Ventralis intermedius (Vim) DBS is an established intervention for medication-refractory essential tremor. Newer constant current DBS technology offers theoretical advantage over the traditional constant voltage systems in terms of delivering a more biologically stable therapy. There are no previous reports on the outcomes of Vim constant current DBS in the treatment of essential tremor. Here we report on the long-term effi-

cacy of Vim constant current DBS in patients diagnosed with essential tremor.

Methods: Essential tremor patients implanted with constant current DBS for a minimum of 3 years were evaluated. Clinical outcomes were assessed using the Fahn–Tolosa–Marin (FTM) tremor rating scale at baseline and postoperatively at the time of evaluation. The quality of life in the patients was assessed using The Quality of Life in Essential Tremor (QUEST) questionnaire.

Results: Ten (10) patients were evaluated, with a median age at evaluation of 74 years (range 66–79) and a mean follow up time of 49.7 (range 36–78) months since starting stimulation. Constant current Vim DBS was well tolerated and effective in all patients with a mean score improvement from 50.7 ± 5.9 to 17.4 ± 5.7 ($p = 0.0020$) in the total FTM rating scale score (65.6%). Furthermore, the mean scores in each of the QUEST domains were significantly reduced (all p values < 0.025) as follows- physical: from 27.8 ± 2.0 to 9.3 ± 1.7 (66.5%); psychosocial from 17.3 ± 0.9 to 5.0 ± 1.6 (71.1%); communication from 4.3 ± 0.9 to 1.3 ± 0.4 (69.8%); hobbies from 6.8 ± 0.7 to 3.6 ± 0.9 (47.0%).

Conclusion: This is the first study to report that long term constant current controlled Vim DBS is a safe and effective intervention for essential tremor, which provides long lasting and marked benefits.

#8582

The Effect of Amantadine on the Dose of Levodopa Required after Deep Brain Stimulation for Parkinson's Disease

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Keywords: Amantadine, Deep brain stimulation, Parkinson's disease.

Background: Deep brain stimulation (DBS) of the subthalamic nucleus for Parkinson's disease has been found to result in significant symptomatic improvements that reduce the need for anti-parkinsonian medications. Interest has been developing around the possibility of a synergistic effect between amantadine and DBS that may provide further symptomatic relief.

Objectives: The primary objective was to investigate the effect of amantadine administration on the dose of levodopa medications required after DBS. The secondary objective was to analyse the stability of the levodopa equivalent dose (LED) over time with DBS.

Method: We undertook a retrospective review of pre and post-operative clinic letters for 158 patients who underwent DBS of the STN in a tertiary referral centre between October 1999 and January 2014. LEDs were calculated using recently published conversion values.

Results: Patients who received amantadine postoperatively (n = 36) had significantly lower doses of levodopa drugs than those who did not receive amantadine (median 288 vs. 525, $p < 0.001$). However this group also received significantly higher doses of non-levodopa drugs (300 vs. 60, $p < 0.001$). The overall LED doses did not differ significantly between the two groups ($p = 0.664$). An analysis of the stability of LEDs over time included 197 follow-up points ranging from 5 months to 7 years postoperatively, each calculated as the change from preoperative LED, showed no significant trend towards an increase in medication (Rho=-0.011, $p = 0.874$).

Conclusions: Amantadine, in addition to DBS, may be beneficial in reducing parkinsonian symptoms enough to allow the substitution of levodopa medications with alternative antiparkinsonian medications. Over a 7 year postoperative follow-up period the LEDs remained stable which supports the idea that DBS may produce a neuromodulatory effect.

#8594

Deep Brain Stimulation Changes Iron Metabolism in Patients with Parkinson's Disease

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Keywords: Deep brain stimulation, Parkinson's disease, Iron metabolism.

Background: Alterations in iron homeostasis can progress towards the development of Parkinson disease (PD) due to accumulation of the iron in the substantia nigra. Deep brain stimulation (DBS) is approved effective method of management of motor symptoms of Parkinson's patients. DBS delivers a constant low, electrical current to a small region of the brain through implanted electrodes. The aim was to evaluate changes in iron metabolism in PD patients after deep brain stimulation.

Material and Methods: Examined group consisted of 10 patients with PD and 1 patient with dystonia who underwent unilateral implantation of STN electrodes in 10 PD cases and 1 GPi electrode in dystonia of deep brain stimulators. Iron, ferritin and transferrin blood levels were assessed before and at least 12 hours after the commencement of deep brain stimulation on standard parameters.

Results: Mean blood serum iron concentration before the electric stimulation was 13.67 umol/l and in period on stimulation was 8.27 umol/l. The reduction of iron concentration after the electric stimulation was statistically significant $p = 0.007$. After overnight of electric stimulation an increase of blood ferritin concentration was observed (122 ng/ml before) and (150.5 ng/ml after)($p = 0.084$), statistically significant reduction of transferrin concentration from 2.39 to 2.17 g/l ($p = 0.024$) and reduction of transferrin saturation from 23.17% to 15.04% ($p = 0.016$).

Conclusion: These results of the pilot study suggest that DBS by delivering electric current, changes the bioelectrical processes and alternates the iron metabolism in patients with PD. It could suggest that deep brain stimulation not only improves motor symptoms of PD but may also influence on pathogenesis of this disease, which is associated with proper iron homeostasis.

#8599

Long-Term Follow-Up of Patients' Quality of Life and Expectations in Subthalamic Nucleus Stimulation for Parkinson's Disease

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Keywords: Expectations, Satisfaction, Subthalamic nucleus stimulation.

Objectives: To prospectively assess the long-term outcome of subthalamic nucleus (STN) deep brain stimulation (DBS) in patients with Parkinson's disease and any relationship with patients' expectations and satisfaction.

Design: STN stimulation is well-established in the treatment of patients with advanced Parkinson's disease. It produces objective improvements in motor symptoms and health-related quality of life. Patient satisfaction with surgical intervention, however, is variable and may be influenced by their individual expectations.

Methods: Nineteen consecutive patients undergoing STN DBS completed a modified 39-item Parkinson's disease questionnaire (PDQ-39) before surgery and at early (6 months) and late (mean 6 years, 4–7) follow-up. A satisfaction questionnaire was included in the post-operative assessment.

Results: At 6 months, most patients expressed satisfaction and felt that surgery had fulfilled their expectations (mean scores of 75.3 ± 17.8 and 73.3 ± 25.3 on a visual analogue scale from 0 to 100) despite a significant difference between expected and actual change (median PDQ-39 summary scores of 24.0, interquartile range 15.0, and 14.0, interquartile range 22.5, respectively, $p = 0.008$).

This was sustained over time with 14 long-term responders declaring their expectations fulfilled (mean score of 85.4 ± 14/5). The main predictor of sustained satisfaction was younger patient age ($p = 0.02$). The mean patient age was 59.8 years with a median disease duration of 11 years. 2 patients had developed advanced dementia at long-term follow-up.

Conclusion: Patient satisfaction correlated with fulfilment of their expectations ($r = 0.910$, $p < 0.001$) rather than quantitative changes in the PDQ-39 scores. This suggests that managing patient's expectations both pre- and post-operatively may be crucial in determining the overall outcome of STN stimulation in Parkinson's disease. Time does not appear to adversely affect patient satisfaction with STN stimulation and its impact on their quality of life.

#8612

Bilateral Pallidal Deep Brain Stimulation versus Bilateral Pallidotomy in the Management of Secondary Postanoxic Generalized Dystonia, A Comparative Study

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Keywords: Dystonia, Pallidotomy pallidal deep brain stimulation.

Background: Secondary post-anoxic generalized dystonia is a common cause of disability especially in socioeconomic settings that lead to improper perinatal care, bilateral Pallidal deep brain stimulation (DBS) and bilateral pallidotomy has been shown extremely effective in treating primary dystonia, however, in secondary dystonias, the clinical effects of bilateral Pallidal DBS and also of bilateral Pallidotomy has been only infrequently described, our aim is to compare the clinical effect and the safety of bilateral Pallidal DBS and simultaneous bilateral posteroventaral Pallidotomy in patients with secondary post-anoxic generalized dystonia.

Methods: 11 patients diagnosed with secondary postanoxic generalized dystonia were treated 5 with bilateral Pallidal DBS and 6 with bilateral Pallidotomy, the change in the severity of dystonia after one year was compared in both groups by Burke–Fahn–Marsden dystonia rating scale, both movement score and disability score (MS, DS respectively), complications especially speech, dysphagia, visual field defects were also compared.

Results: The BFM scores improved significantly in both patient groups after 1 year, the MS by 42 ± 4.6 in the DBS group and by 40 ± 2.3% in the Pallidotomy group and the the DS improved by 32 ± 4.9 in the DBS group and by 26 ± 6.2% in the pallidotmy, however no statistical significance was found in the improvement in both groups, two patients in the Pallidotomy groups and one patient in the stimulation group had visual field affection, one patient in the stimulation group had infection that necessitated removal of the entire system, speech complications occurred in a single patient from the Pallidotomy group.

Conclusion: Both bilateral Pallidal deep brain stimulation and bilateral Pallidotomy are equally effective in the treatment of secondary post-anoxic generalized dystonia with the Pallidal DBS having potentially less adverse effects.

#8672

Initial Implantation of Rechargeable IPGs in DBS Patients with Movement Disorders: User Confidence and Satisfaction, Evaluation of Recharging and Adverse Events

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Keywords: Rechargeable IPG, Deep brain stimulation, Movement disorder.

Introduction: Rechargeable internal pulse generators (IPGs) for deep brain stimulation (DBS) have been available for several years now. Smaller implant size and longer battery life of 9 years or more are advantages offered by rechargeable IPGs. However no guideline exist with regards to implanting a rechargeable IPG during the initial surgery, or in case of battery replacement or choice. Furthermore it is unclear how to preoperatively assess a patient's abilities to properly use and take care of a rechargeable IPG. Little data exists on how the recharging process influences the patient's life. The objective of this study is to generate data on the impact of the rechargeable IPG on their life as well as the patients' satisfaction adverse events and assessment of the recharging process in our patient population with movement disorders that had a rechargeable IPG placed during their initial DBS surgery.

Material and Methods: 35 patients consecutive adult patients with movement disorders that underwent DBS surgery with implantation of a rechargeable Brio IPG from 2012 to 2015 received a questionnaire and were asked to answer questions regarding their recharging routine, their user confidence and satisfaction, their recharging routine, their assessment of the recharging process, their life with a rechargeable IPG and their use of technology in everyday life. The overall recharging process as well as the different steps of it (checking IPG battery status, putting on antenna & recharging belt, conencting antenna & IPG, keeping antenna & IPG connected, charging the charger) were assessed on an ordinal scale (5 = very easy, 4 = easy, 3 = moderate, 2 = difficult, 1 = very difficult).

Results: The questionnaire return rate was 89% (n = 31 patients). N = 21 Patients suffered from Parkinson's disease (PD), n = 8 suffered from essential tremor (ET) and n = 2 patients had dystonia (DY). Mean age was 63.3 years (±11.8 years, 32–78 years) and mean time since surgery was 21.2 months (± 10.0 months, 5–41 months). 77.4 (n = 24) patients recharge their IPG themselves. On average 1.65 (±0.87) training sessions were given to the patients after which 71.0% felt sufficiently confident in using the rechargeable IPG. At the time of the survey 90.3% felt confident using the rechargeable IPG. N = 3 patients (all PD patients) did not feel confident. The same number of patients experienced events of inability to recharge their IPG. Lack of user confidence was highly significantly associated with inability to recharge their IPG ($p < 0.001$). N = 1 patients experienced unintended interruption of stimulation after inability to recharge and n = 5 additional patients had interruption of stimulation for other reasons. Neither age, neurological disease, user experience or use of technology (Cellphone, tablet, desktop PC) in everyday life was significantly associated with adverse events. However patients able to driva a car were highly significantly less likely to experience lack of user confidence or inability to recharge ($p < 0.001$, $p = 0.01$). The recharging process (4.0 points) as well as the individual steps (3.7–4.2 points) were rated as 'easy'. 96.8% of patients are satisfied with their rechargeable IPG and 93.5% of patients would recommend a rechargeable IPG over a non-rechargeable model. Age, neurological disease and user experience do not significantly influence the overall rating.

Discussion: This study provides data on the largest group of DBS patients with initial implantation of a rechargeable IPG reported so far. Patient satisfaction and user confidence is high in patients with rechargeable IPGs as their initial neurostimulator. Patients of advanced age (≥70 years) are also able to learn to securely use a rechargeable IPG. Even when the patients do not perform the recharging process themselves, rechargeable IPGs can be considered for implantation safely. Interestingly the use of technological devices such as cellphones did not positively correlate with a better rating or less adverse events. Patients able to drive a car felt most confident using their IPG and were least likely to experience inability to recharge. As driving a car represents a more complex task than using a cellphone it can be assume that these patients have best overall functional status and therefore less problems. While our study is retrospective it is up to a future prospective trial to make recommendations for screening questions or tests to safely assess the patients capability to use a rechargeable IPG.

#8773

Preliminary Experience of Thalamotomies Induced by a Trans-Cranial MRI-Guided Focused Ultrasound Surgery (tcMRgFUS) System Operating at 1.5 Tesla, in a Series of Tremorigen Patients Not Suitable for DBS

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Keywords: tcMRgFUS, Essential tremor, Ultrasound lesion.

Background: Functional neurosurgery was born and grew up with lesioning procedures but in these last two decades deep brain stimulation (DBS) has almost completely replaced these

techniques. Nevertheless, there may be still patients that specifically benefit from lesioning procedures or may not be suitable for DBS techniques. (1,2,3). We report our preliminary experience of thalamotomy by trans-cranial MRI-guided Focused Ultrasound Surgery (tcMRgFUS) installed on a 1.5T MRI unit, in a consecutive series of 8 tremorigen patients.

Methods: 8 patients, 7 males and 1 female, age ranging from 35 to 78, were previously evaluated, and Essential Tremor (ET) (7 cases) or a tremorigenic form of Parkinson Disease (PD) (1 case) was diagnosed. Two male patients with ET showed also a head tremor. One of them had a dystonic form of ET. In all cases, DBS was excluded for several reasons, including clinical contraindications or patient decision to deny informed consent for an open skull surgical procedure. Screening brain CT and contrast enhanced MRI were performed to individuate the suitable patients in relation to their skull parameters (skull density ratio, SDR). Co-existing pathological cerebral findings were also considered as an exclusion criterion. The decision to choose a specific side to be treated was determined by the side were tremor was prevalent, or by the patient preference. In the two cases of axial tremor, we decided to treat the driving side, which was considered the one with a more ancient history and maybe a more evident clinical expression. No patient had bilateral treatment even if insistently required by the patient. Gradually higher intensity ultrasound sonications were delivered after meticulous target positioning was determined considering stereotactic atlases and individual brain anatomy disclosed by pre-operative neuroradiological exams. After stereotactic frame positioning, the patients lied on a dedicated MRI table with the head inside the tcMRgFUS helmet. T2w high resolutions (2 mm thick, no gap) MRI sequences were acquired to guide the procedure and then sonications of progressively higher intensity were delivered causing increasing heating of the selected area to identify the best target for this specific patient. Low energy allowed to achieve a clinical benefit without inducing a permanent brain lesion. Once sure that the targeted area was optimal, a few sonication with higher energies were delivered to induce a permanent lesion on the ventralis intermedium nucleus (VIM) of the thalamus. During each step of the procedure the patients were strictly clinically monitored. In one case of ET with a dystonic component and a coexisting head tremor, there was the need to sonicate the left VIM more laterally respect to the prefixed target.

Results: Symptoms relief was immediate and continuous real-time neurological evaluations excluded any motor or sensitive deficit. When necessary, the focus beam was also adjusted by slightly shifting the transducer 1 mm in the desired direction, to precisely shape the lesion itself. The treatment was uneventful, with almost complete relief of the symptom in all patients. The effect was consolidated after 24 hours. A 48 hours contrast enhanced brain MRI showed the lesion as stable, without surrounding bleeding spots neither other complications. In the case of the dystonic tremor that was treated more laterally, a slight motor impairment to the right hemisoma occurred a few days after the treatment. Otherwise this symptom showed a spontaneous and prompt relief with complete recovery within one week. Surprisingly even the axial tremor was immediately relieved after treatment by lesioning the driving side thalamus.

Conclusions: Even if DBS may remain the most frequent procedure to treat disorders as Parkinson disease and essential tremor, MR-guided focused ultrasound may be an added available tool in the armamentarium of the functional neurosurgeon. It's way of generating intracranial lesions in a non-invasive matter providing an immediate relief to the patients is really appealing. Although this is a preliminary experience, the clinical success of our first treatments proves that this promising new technology for non-invasive treatment of various brain disorders can be safely and effectively performed also with the most popular MRI units operating at 1.5T.

#8775

Altered FDG Metabolism by Subthalamic Deep Brain Stimulation in Patients with Parkinson's Disease

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Keywords: PET, Subthalamic nucleus, Deep brain stimulation, Parkinson's disease, FDG.

Objective: The objective of this study was to apply the Parkinson's disease-related pattern (PDRP) as a measure of network biomarker of evaluating Parkinson's disease (PD) patients with the treatment of subthalamic (STN) deep brain stimulation (DBS) by using 18F-fluorodeoxyglucose (FDG) and Positron Emission Tomography (PET).

Methods: Resting-state brain FDG PET imaging was performed in 8 PD patients and 8 healthy controls to identify a PDRP. After the operation of STN DBS to PD patients, the PDRP was evaluated either.

Results: Relative to healthy controls, the PDRP increased obviously in PD patients, the STN DBS inhibited the PDRP ($P < 0.05$) accompanying by the improvement of motor function ($P < 0.05$). The alleviation of rigidity was associated to reduce of PDRP ($P < 0.05$). The FDG in occipital decreased remarkably in PD patients compared with healthy controls ($P < 0.05$), meanwhile, the FDG in frontal and putamen increased obviously ($P < 0.05$). The FDG in parietal and occipital lobes was raised up by the treatment of STN DBS ($P < 0.05$), and then the FDG in frontal lobe and putamen was reduced ($P < 0.05$). The alleviation of rigidity correlated to the FDG increment of the parietal lobe ($P = 0.014$). Furthermore, the decrease of the PDRP correlated to the inhibition of the FDG activity of putamen ($P = 0.003$) and the increase of the FDG activity of occipital lobe ($P = 0.001$).

Conclusion: STN DBS improves the motor function by adjusting the dysfunctional activity of the motor circuit of PD patients. PDRP is sensitive biomarker of the motor circuit of PD patients; it could be utilized to evaluate the outcome of treatment of STN DBS to PD patients.

#8804

Anatomical Landmarks for Deep Brain Stimulation Shift

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Keywords: STN, GPi, AC-PC, 3rd Ventricular width, Intraoperative brain shift.

Introduction: The effectiveness of intraoperative measures to avoid brain shift in Deep Brain Stimulation surgery is still to be proven. Our aim is to assess bran shift in the presence of these measures and to identify anatomical landmarks that help to predict it.

Methods: Retrospective cohort study of Parkinson Disease (PD) and Dystonia (DYST) patients admitted for DBS surgery (January 2013-January 2015) in a single centre. STN and GPi stereotactic coordinates, the implanted electrode, the chronic stimulated pole, the first site to be implanted and the time between eletrodes placement were evaluated for each patient. AC-PC, 3rd Ventricular width and vertical diameters and the distance between both temporal and frontal horns were evaluated in the pre-op MRI for each patient.

Results: 42 patients were considered (14 DYST and 28 PD; 84 nuclei evaluated – 28 GPi and 56 STN). The mean values of each coordinate were right GPi (X- 21.38 ± 0.53; Y- 0.66 ± 0.47; Z- –1.59 ± 0.55), left GPI (X- –18.13 ± 3.25; Y- 0.28 ± 0.48; Z- –2.67 ± 0.50), right STN (X- 12.53 ± 0.53; Y- –1.91 ± 0.16; Z- –4.29 ± 0.22) and left STN (X- –12.31 ± 0.52; Y- –2.06 ± 0.20; Z- –4.56 ± 0.13). The adjusted analysis revealed that the X coordinate variate bilaterally and consistently (STN and GPi) with the distance between both temporal horns. Left electrode was the first to be placed in 52.8% (n = 19) of the cases. Time difference between the first and second electrode placement was 132.5 ± 4.6 minutes (no difference between DP and DYST). Central electrode was placed in 66.7% (n = 16) – left side – and 52.2% (n = 12) – right side – of the cases. The second pole (counting from the extremity) was the most frequent in chronic stimulation (left – 44.4%, n = 8; right – 52.6%, n = 10). Although the unadjusted analysis showed no difference between the first and the second implanted eletrodes, the ventricular dimensions adjusted analysis revealed an increase AC-PC and 3rd Ventricular width produces a more anterior and medial contralateral final electrode with no variation in the chronic stimulated pole ($p < 0.05$). There was no influence of the vertical dimension in either electrode or chronic stimulated pole in the second implanted site. ($p > 0.05$).

Conclusion: STN and GPi X coordinate variates with the distance between both temporal horns. AC-PC and 3rd Ventricular width influenced the final position of the second implanted electrode. Both findings support CSF as an important player in intraoperative brain shift.

#8878

How Does Vagal Nerve Stimulation Alter Functional Connectivity? Study Based on Intracerebral Recordings and Comparison Between 'On' and 'Off' Stimulation Periods

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Keywords: Vagal nerve stimulation, SEEG, Functional connectivity.

Introduction: The mechanisms of the anti-epileptic action of vagal nerve stimulation (VNS) are still poorly understood. An effect of VNS on cortical synchronization has been postulated but remains to be demonstrated. In this study, we investigated the impact of VNS on functional connectivity (Fc) using direct intracerebral recordings of several cortical areas (SEEG) by comparing the 'on' versus 'off' stimulation periods.

Material and Methods: Five patients with drug resistant epilepsy who underwent SEEG recordings during ongoing VNS therapy were investigated. Four patients were regarded as non responders to VNS whereas one was deemed responder (>50% seizure decrease). SEEG signal was acquired during 30 min periods of time and interdependencies (co-occurrence of signal) between twenty-six selected bipolar SEEG channels from different cortical areas were estimated by nonlinear regression analysis based of h^2 coefficient. Comparisons were performed during 'on' and 'off' periods of stimulation. The parameters were similar to those chronically used for the patients (Amplitude 0.75–3 mA; pulse width 0.5 ms; Frequency 50 Hz). For three patients different stimulation amplitude were also tested. Stimulation artefacts were detected with the help of two additional cutaneous cervical and upper thoracic electrodes. Levels for significance were adjusted according to Bonferroni's method to counteract the problem of multiples comparisons (increased risk of type 1 error).

Results: In comparison with 'off' periods, the 'on' periods disclosed significantly higher values (increased Fc) for four patients (P1, P3, P4, P5) and lower values for one patient (P2). From thresholded graphs, we observed increased connections between several brain regions in P1 and P5 and decreased connections in P2. Finally, the only decreased Fc occurring during VNS corresponded to the responder patient suggesting that the effect might be related to this mechanism.

Conclusion: Our study suggests that VNS does alter the functional connectivity but in a complex, inconstant and varying way. It also shows a high degree of regional variability of the effect. The only patient in whom the functional connectivity was found to be decreased turned out to be the only patient deriving a benefit from VNS. The study is too preliminary to draw any solid conclusion but the mechanisms of action may involve a decrease in Fc. These results are consistent with the existing literature showing a decreased functional connectivity of interictal activity during

VNS in responders on surface EEG. This is the first study showing alterations of functional connectivity in VNS patients based on deep intracerebral recordings. The regional specificities and the optimal parameters associated with these effects are still to be determined.

#8881

Functional Electrical Stimulation (FES) of the Peroneal Nerve for Patients with Parkinsons Disease and Freezing

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Keywords: FES, Parkinsons disease, Freezing.

Introduction: Freezing of gait (FOG) remains a significant problem for patients with Parkinson's disease (PD). Whereas Deep Brain Stimulation (DBS), as well as dopaminergic medical treatment is able to reduce the cardinal symptoms of PD, such as tremor, rigidity and bradykinesia, the effects on FOG remain limited. A number of different kinds of treatments (conservative and surgical) have been tested within the recent years to treat FOG. Such as DBS in the PPN, queing and many more.

Methods: 3 patients with FOG due to PD (1 with and 2 without DBS) have been treated by FES via an external device. This device is activated via a mechanical sensor in the shoe of the patients if the FOG starts and the patients start to get propulsion.

Results: After a testing phase of several days, the patients got the device for a permanent treatment. With a follow-up time of 1–3 years, all patients are still profiting from this treatment. The number of falls could be significantly reduced. Stopping the stimulation leads in all cases with a differential delay (between several hours and up to 1 day) again to the FOG symptoms. We have seen that far no side effects due to this treatment. Videos with/out stimulation will be shown during the presentation.

Discussion: FES of the peroneal nerve with a feedback coupled system reacting to propulsions by an external stimulating system may be an effective and non invasive treatment modality for FOG in PD patients. The effects may be longlasting. However a controlled trial will have to be performed.

Oncology

#8584

A Multipurpose Guidance Probe for Stereotactic Biopsy Procedures

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Keywords: 5-ALA, Fluorescence spectroscopy, Laser doppler flowmetry (LDF), Brain tumour, Optical biopsy.

In the routine of biopsy sampling from suspected tumors located deep in the brain, biopsies are harvested using a stereotactic neurosurgical procedure and then sent for pathological investigations to obtain a preliminary diagnosis within 1–2 hours. The biopsy is then further examined for a definitive assessment within 2 weeks before postoperative oncological treatment is decided. Biopsies are taken from pre-calculated sites based on the preoperative radiologic images. During biopsy the location of the tumor may vary due to brain shift making diagnosis less accurate. In such cases the biopsy procedure needs to be repeated leading to a longer operation time. The perioperative risks are hemorrhage (5%), infection and seizure (0.5%). The morbidity rate has been reported to be 7% where about 88% is related to the hemorrhage [1].

In order to provide a more precise guidance for locating the most probable tumor sites and to avoid hemorrhage in the biopsy channel, a multipurpose fiber optic probe has been developed. The probe detects and quantifies the 5-ALA (20 mg/kg) induced protopophyrin IX (PpIX) fluorescence in the tumor using a fluorescence spectroscopy system (FSpect) and microvascular blood flow using a laser Doppler flowmetry (LDF) system. The probe was inserted in the same planned biopsy trajectory prior to the biopsy needle and the recorded signals were compared to the histopathology diagnosis of the samples taken and as well to the preoperative radiologic images. The fluorescence system has previously been used during approximately 50 high grade glioma resections [2, 3] and the LDF was used as a 'vessel tracking' tool in over 120 stereotactic deep brain stimulation (DBS)-lead implantations [4].

The multipurpose probe has successfully been utilized in four stereotactic biopsy procedures at the Neurosurgical Department in Linköping University Hospital. On all occasions clear and strong fluorescence peaks were visible in real-time in the operating room.

These values in the earlier evaluation of the system during brain tumor resection [2] corresponded to high grade glioma tissue. The peaks gradually increased when the probe was inserted deeper into the tumor tissue. No high blood flow spots i.e. vessels were seen along the trajectories. Figure represents the post-processed optical signals for one of the occasions with fluorescence signals along the insertion trajectory. All together 73 LDF and 28 fluorescence recordings were made, and 3 biopsies were taken. The biopsy samples were diagnosed as reactive glial cells with tumor cells (biopsy 1), glioma grade IV tumor (biopsy 2 and 3) which confirmed the fluorescence signals.

In conclusion, the multipurpose guidance probe makes direct detection of fluorescence possible during the biopsy procedure. This can help in defining the position for the biopsy and give a direct feedback of malignancy. The LDF part of the guidance technique help track high blood flow spots along the trajectory. However, more investigations are necessary in order to proof the concept.

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Pain

#8389

New Neuromodulation System for Peripheral Nerve Stimulation: Efficacy on Pain and Mental Status

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Keywords: Peripheral nerve stimulation – pain – SF-36.

Objective: To evaluate 31 patients suffering from drug resistant neuropathic pain due to only one peripheral nerve damage and treated by new dedicated device for peripheral nerve stimulation (PNS).

Materials and Methods: The evaluation was on pain using the Numeric Rating Scale (NRS) and on mental status component (MSC) using the SF-36 at baseline and at median follow-up (18 months) after implant.

Results: The NRS baseline score was 8.9 ± 1.1 and at last follow-up 3.6 ± 2.2 with an improvement of the 59.7% ($p < 0.001$); the MSC of the SF-36 started fron a baseline score of 36.4 ± 11.5 to a follow-up score of 45 ± 9.6 ($p < 0.05$) with improvement of the 23.8%.

Conclusions: This new device has been able to improve statistically the NRS and the MCS of the SF-36 scores with a clinical reduction of the pain and an increase of the mental status.

#8404

Occipital Nerve Stimulation Improves the Global Health Status in Medically-Intractable Chronic Cluster Headache

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Keywords: Cluster headache, Occipital nerve stimulation, Quality of life.

Background: Occipital nerve stimulation (ONS) has been proposed to treat chronic medically-intractable cluster headache (iCCH) in small series of cases without evaluation of its functional and emotional impacts.

Methods: We report the multidimensional outcome of a large series of iCCH patients, treated by ONS within a french-speaking multidisciplinary network (clinicaltrials.gov NCT01842763), with a one-year follow-up. Prospective evaluation was performed before surgery, then three and twelve months after.

Results: One year after ONS, the attack frequency was decreased >30% in 64% and >50% in 59% of the 44 patients. Mean (Standard Deviation) weekly attack frequency decreased from 21.5 (16.3) to 10.7 (13.8) ($p = 0.0002$). About 70% of the patients responded to ONS, 47.8% being excellent responders. Prophylactic treatments could be decreased in 40% of patients. Functional (HIT-6 and MIDAS scales) and emotional (HAD scale) impacts were significantly improved, as well as the global health status (EQ-5D). Mean (SD) EQ-5D visual analogic scale score increased from 35.2 (23.6) to 51.9 (25.7) ($p = 0.0037$). Surgical minor complications were observed in 33% of the patients.

Conclusion: ONS significantly reduced the attack frequency, the functional and emotional headache impacts in iCCH patients and dramatically improved the global health status of responders.

#8466

Deep Brain Stimulation Targeting the Thalamic Cavity Wall in a Rat Model for Thalamic Syndrome

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Introduction: The thalamic syndrome, first described by Dejerine and Roussy, is a central neuropathic pain syndrome occurring after thalamic stroke, often associated with a mild paresis. It is a form of central post-stroke pain. Treatment is challenging and often not satisfying.

Material and Methods: 30 rats were tested for thermal and mechanical pain and motor performance, and were then randomly allocated into an experimental group (E; electrolytic thalamic lesioning; $n = 22$) and a control group (C; sham surgery; $n = 8$). Pain and motor tests were repeated weekly over the next 4 weeks. Next, after CT and MR imaging, 3 bipolar electrodes were implanted. E was randomly divided into a cavity wall electrode group (W; electrodes aiming for the ventral cavity wall; $n = 11$) and a random electrode group (R; electrodes aiming for a random brain target not related to motor or pain behaviour; $n = 11$). In C, electrodes were implanted at the same coordinates as in W. Motor tests were then repeated during deep brain stimulation (DBS; biphasic, 130 Hz, 200 µs at 0%-50%-75%-100% of the highest tolerated amplitude (HTA; amplitude above which side effects are observed)).

Results: After but not before lesioning, motor scores were significantly ($P < 0.05$) worse in E vs. C, while pain scores did not differ. In W, DBS at 50%, 75% or 100% HTA did not improve motor scores significantly as compared to 0% HTA in W or to DBS in R or C.

Conclusion: In a thalamic syndrome rat model with motor deficits but no mechanical or thermal hyperalgesia, the tested DBS parameters did not alleviate symptoms.

#8566

rTMS Therapy on M1 Modifies the Motor Map in Chronic Neuropathic Facial Pain – A Pilot Study

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Keywords: Mapping, Motor cortex, Navigated transcranial magnetic stimulation.

Introduction: Repetitive transcranial magnetic stimulation (rTMS) targeted to primary motor cortex (M1) has been proven effective in treating therapy-resistant chronic neuropathic pain

(Lefaucheur et al, 2014). However, the mechanisms of action of rTMS are so far unknown, though probably at least partly shared with epidural motor cortex stimulation (MCS). TMS can be used to assess the excitability of the cortex (resting motor threshold, rMT) and corticospinal inhibition (silent period duration). Previously, defective inhibition has been described in chronic neuropathic pain (Lefaucheur et al, 2006). As well, neuroplastic changes have been observed in sensory-motor areas (Krause et al, 2006).

Objectives: We hypothesized that there are changes in the excitability or motor map configuration in chronic pain. In addition, we studied whether these changes normalize after two 5-days rTMS treatment sessions separated by 6 weeks. Therapy was targeted to the somatotopic facial primary motor cortex using neuronavigated TMS.

Patients and Methods: Six patients with severe unilateral, chronic atypical facial pain were enrolled in the study. High-frequency rTMS (randomized to 10 Hz or 20 Hz, 2400 or 3600 pulses per session, 90% of the rMT) was targeted to functional motor representation area of the lower face (mentalis or orbicularis oris muscle). The optimal stimulation site for face and hand was assessed and rMTs determined on both hemispheres. Silent period duration was measured on the hand muscle. Motor areas corresponding to the painful side were mapped using 105% of the rMT. The area and the center-of-gravity (CoG) of the map were determined.

Results: rTMS sessions did not significantly change the rMTs of either hand or face on either hemisphere. However, there was a trend of interhemispheric difference decrease in rMT of the face after rTMS ($p = 0.229$, paired t-test). There was no difference in the sizes of the representation areas though they were individually slightly altered in shape. The CoGs moved laterally in all patients and posteriorly in all but one patient (non-significant). There was a trend of increase in the duration of the silent period ($p = 0.060$, paired t-test).

Conclusion: No statistically significant changes were observed in the excitability, though corticospinal inhibition seemed to normalize after rTMS treatments. These preliminary results suggest that rTMS induces slight changes in the motor map plasticity measurable 4–10 days after last rTMS treatment session. These may have potential implications in better tailoring of rTMS treatment for chronic pain and for efficient placing of the MCS electrode.

Psychiatric Disorders

#8488

Experience with Anterior Capsulotomy in Obsessive-Compulsive Disorder

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Keywords: Obsessive-compulsive disorder, Anterior capsulotomy, Thermolesion.

Objective: Stereotactic anterior capsulotomy (AC) is a possible treatment method in patients suffering from intractable obsessive–compulsive disorder (OCD).

Methods and Patients: Encouraged by the results of other centers, we performed bilateral AC in 7 patients (F:M = 3:4, mean age 41 yrs, SD ± 7.7, disease duration ≥5 yrs) with a severe form of OCD, in whom conservative psychiatric treatment had failed (pharmacology and other therapeutic alternatives). All patients were indicated by a psychiatric and neuropsychological committee independently of neurosurgeons. The Yale-Brown Obsessive Compulsive Scale (Y-BOCS; range 13–36, mean 29.5, SD ± 8), cognitive tests (AVLT, ROCFT, WAIS-R/III, Verbal fluency test – phonemic, TMT A/B) and mood/emotional disorders scales (MADRS, BDI-II, BAI, SQUALA, SF-36) were performed in all patients prior to and 1 year after surgery. The Leksell Sterotactic Frame, SurgiPlan Software (Elekta) and T1- (post-contrast) and T2-weighted sequences acquired at 1.5 T (Siemens Avanto) were used for target localization. Two (5 patients) to three (2 patients) thermolesions (78–85°C/60 s) were applied in the bilateral anterior internal capsule (AIC). First the deepest lesion was localized: X = 14–16 mm lateral to midline, Y = 8–10 mm anterior to the posterior border of the anterior commissure, and Z=the level of the foramen of Monro. The second and third lesions were seated in the AIC towards the periphery, 5 mm apart from each other.

Results: Surgery was successful in 4 patients in whom the Y-BOCS significantly decreased (by 76.9%, 72.4%, 35.4%, 25.6%). Two of these patients with the least improvement (35.4%, 25.6%) and with 2 lesions on each side underwent enlargement of the previous lesions and Y-BOCS additionally decreased by 9.7% and 7.7%, respectively. Two patients have not completed one year follow-up and 1 patient refused post-surgical assessment. No neurological or neuropsychological deficits have been observed.

Conclusion: In our limited experience, AC surgery was a safe and effective procedure for OCD. Although our sample was small, our results may positively contribute to the debate regarding the suitability of AC for refractory OCD.

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#8801

Acute Fornix DBS Induces Long-Term Depression of Hippocampal Synaptophysin Levels

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Introduction: Deep brain stimulation (DBS) of the fornix can restore memory functions in animals with experimental dementia. We have shown that one potential underlying mechanism is the enhanced release of acetylcholine in the hippocampus. Another suggested mechanism of action is neuronal plasticity.

Objective: Here, we have tested the hypothesis that acute fornix DBS can have long-term beneficial effects on memory by enhancing histological parameters of neuronal and synaptic plasticity.

Materials and Methods: Rats were implanted with bilateral electrodes at the site of the fornix and received DBS at 100 Hz, 100 μA and 100 μs pulse width for 4 h. Three days after stimulation, rats received BrdU injections twice daily for a period of 3 days. After 5 weeks, fornix DBS and sham rats were tested in the water maze task. Probe trials were given after 1 h and 48 h. About 6.5 weeks after DBS, rats were sacrificed and their brains processed for BrdU/NeuN, p-CREB or synaptophysin immunohistochemistry.

Results: Fornix DBS rats visited the target annulus more frequently than sham rats in the probe trial with 1 h delay. We did not find any differences for the number of double-labelled BrdU/NeuN or p-CREB cells for fornix DBS rats when compared to sham. Synaptophysin-immunoreactive presynaptic boutons, however, were significantly decreased in the CA1 and CA3 subfield of the hippocampus for fornix DBS rats when compared to sham.

Conclusion: Fornix DBS enhances long-term spatial memory independent of the neuroplasticity markers, which were used in the present study. An interesting finding is the decrease in the synaptic-neuroplasticity marker, which might suggest a long-term depression related mechanism.

Spasticity

#8316

The Role of Volume in the Effectiveness of Intrathecal Baclofen. First Proof of a Saturation Point?

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Keywords: Intrathecal, Baclofen, Saturation, Point.

Introduction: The intrathecal application of Baclofen is the most effective way to treat spasticity. The electronic pumps are almost always the ones being preferred when it comes to first implantations although in some cases a constant flow pump is being preferred. The electronic pumps work in microliters were as the constant flow pumps apply much greater volumes. The aim of our study is to examine the role of volume in the effectiveness of intrathecal baclofen.

Methods: In our department we have implanted more than 1200 pumps in patients with all types of spasticity. We treat and refill more than 280 pumps on a regular basis. Out of those, 198 are electronic ones and 82 are constant flow pumps. Out of the 82 constant flow pumps, 46 have an daily Flow of 0.5 ml (0.26–0.6 ml), 29 have an daily flow of 1 ml (0.95–1.2 ml) and 7 have an daily flow of more than 1 ml (1.5–2.1).

Results: Patients with a flow of 0.5 ml had a mean intrathecal dose of 317.5 μg, the ones with a flow of 1 ml had a mean Dose of 620.2 μg and the ones with a flow of more than 1.5 ml had a mean dose of 700 μg. Patients where the tip of the catheter was above the level of T7 and have a flow of 0.5 ml have a mean dose of 426 μg and the ones with a flow of 1 ml have a mean dose of 636 μg. Patients with the tip of the catheter between T8 and T11 and a flow of 0.5 ml had a mean dose of 334.5 μg whereas the ones with a flow of 1 ml had a mean dose of 900 μg. Patients where the tip was under the level of T12 and with a flow of 0.5 ml have an average dose of 475 μg and the ones with a flow of 1 ml have an average dose of 550 μg.

Conclusions: The volume of Baclofen in the intrathecal space plays a deciding role in its' effectiveness. A volume of 0.5 ml seems to be much more effective than a volume of 1 ml or more despite the height of the intrathecal catheter. The data suggests that the smaller the volume the more effective Baclofen is. Moreover it seems that the greater the volume is, the greater the needed dose is, in order to effectively treat spasticity. Keeping in mind that Baclofen has to bind to the GABA Receptors in order to be effective, the studies of Yaksh et al. (1999) and Wallace et al. (1999) and the above mentioned data, these findings sudjest that there is a saturation point of baclofen in the intrathecal space. This fundamentally changes the way we thought baclofen needs to be applied in the intrathecal space in order to reach maximum effectivity and therefor changes the strategy needed to best treat patients with spasticity.

#8540

Spinal Cord Stimulation and Chronic Intrathecal Baclofen Therapy in the Treatment of Drug-Resistant Forms of Spasticity in Patients after Spinal Cord Injury

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Keywords: Spinal cord stimulation, Chronic intrathecal baclofen therapy, Spasticity, Spinal cord injury.

The annual incidence of complicated by spinal cord injury is about 40 cases per million population. Spastic syndromedevelops in 65–78% of patients who underwent severe spinal cord injury during the first year.

The most common method is the implantation of spasticity correction baclofen pump. But this method has a number of drawbacks, such as the permanent filling, the development of severe withdrawal symptoms, which are not peculiar to the stimulation of the spinal cord.

Objective: To compare the chronic intrathecal baclofen therapy (ITB) and the spinal cord stimulation (SCS) for the treatment of spasticity in patients with spinal cord injury.

Materials and Methods: In this study involved 9 people who underwent surgery in September 2014 among them 4 patients implanted system for spinal cord stimulation and 5 patients implanted pump.

The first stage of the patient performs the trial stimulation. If the stimulation mentioned amid tone reduction, to a comfortable level for the patient, the implantation was carried out system for stimulation of the spinal cord. If the patient did not respond to stimulation or could not get comfortable lowering the tone, the patient performs baclofen test. According to the results of which the decision was made about the need to pump implantation.

Results and Discussion: As a result of the treatment in all patients there is a decrease in spasticity. For patients with ITB tone on average decreased by 2 ± 0.3 points on a scale of Ashworth. Patients with SCS marked reduction in spasticity for 1.5 ± 0.3, but unlike patients with ITB they had the possibility of 'dosed' level depending on spasticity everyday activity. That is, whennecessary, patients have the opportunity to raise the level of spasticity to the original, or to reduce it up to 1 b Ashworthscale.

Conclusions: Chronic spinal cord stimulation is a highly effective method of spasticity correction, in some cases not inferior to intrathecal therapy with baclofen.

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Stereotactic and Functional Neurosurgery

Brain Machine Interface and Imaging

#8586

Deep Brain Stimulation Steering of the Electric Field: A Patient-Specific Simulation Study

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Keywords: Deep brain stimulation (DBS), Lead design, Electric field, Computer model, Visualization.

Introduction: Deep brain stimulation (DBS) systems can be operated in voltage and current mode, and the electric field (EF) steered by redesigning the contacts on the leads. The aim of this study was to exemplify the possibilities with patient-specific computer simulations by using the finite element method (FEM) in the investigation of the EF around DBS leads and its influence from tissue type, stimulation mode and active contact surface.

Methods: Two leads with steering function; 6180 (St Jude Medical, USA) and SureStim1 (Medtronics Eindhoven Design Center BV, The Netherlands) and the conventional 3389 lead (Medtronics Inc, USA) were used for the investigation. Both equivalent contact configurations as monopolar settings, and different steering posibilities, were considered. The leads were applied in two brain targets of the same patient i.e. the zona incerta (Zi) where the actual lead was implanted, and a virtually calculated target, the ventral intermediate nucleus (VIM) of the thalamus. The simulation study was approved by the local ethics committe (2012/434–31) and the patient gave informed written concent. A brain model consisting of electrical conductivity values of the grey and white matter, cerebrospinal fluid and blood was created by classifying the preoperative stereotactic 3T MR image with the in-house developed MatLab software [1]. Based on Leksell coordinates, extracted from the postoperative co-registerd CT-MRI lead artefacts in Surgiplan (Elekta Instrument AB, Sweden), the three leads were placed in Zi and VIM in the brain model. Simulations of the EF surrounding each lead and target were done at equivalent amplitudes in voltage and current modes [2] by use of Comsol Multiphysics (Version 5.2, Comsol AB, Sweden). All simulations were done in the chronic stimulation time point corresponding to four weeks post surgery. The results were displayed with 0.2 V/mm isolevels in axial, coronal and sagittal directions. The setting of the isolevel was based on neuron model simulations [3]. The shape, volume and maximal radial distance were calculated for each simulation and compared between stimulation modes, targets and leads with and without steering.

Results: The simulations show that equivalent monopolar contact configurations on the three leads result in similar EF distribution, but with systematic larger volumes in current mode compared to voltage mode. Due to tissue variations in the target region, there was a small difference in volume and shape between the two targets. The volumes were systematically a few percentage larger in Zi compared to VIM. The steering function for lead 6180 is examplified. In these simulations one segment of the split ring (contact 5) of 6180 was set to 3 V and compared to a setting with all three segments active with the same amplitude. In current mode eqvivalent EF isosurface for the steering function was found for an amplitude of 1.1 mA. Additional examples of the steering function and its implications on the EF from stimulation mode and tissue types will be presented in the poster.

Conclusions: Simulations showed that in current mode, smaller contact surface area achieve a larger electric field extension in comparison to voltage mode. The electric field extension is influenced by the surrounding tissue regardless of the operating mode.

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Epilepsy

#8454

The Advantages of Stereotactic Treatment of Patients with Temporal Lobe Epilepsy

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Keywords: Epilepsy, Stereotaxis, Amygdaleum, Hippocampus.

Current data indicate high effectiveness of the surgical treatment of patients with temporal lobe epilepsy. Anterior temporal lobectomy and selective amygdalohippocampectomy are the typical operations in this disease. Stereotactic interventions in the area of a hippocampus and amygdaleum are the alternative to open surgery, and they have a long history. Such operations had a pathophysiological basis; however, in recent years in the world practice, an interest in such interventions almost disappeared. The reason is the relatively low efficacy, compared with the open surgery in these patients.

On the other hand, there are many positive sides in a minimally invasive approach, implemented when performing stereotaxy. Stereotactic interventions are performed under local anesthesia and much smaller in duration, compared with lobectomy. Besides, it was found that a temporal lobectomy may be associated with risk of the growth of cognitive, neuropsychological and visual disorders. In addition, in the cases of lack of effectiveness of stereotaxis, the patients may be performed to repeated stereotactic operations or to an open surgery subsequently.

Now we can talk about the resurgence of stereotactic operations in patients with temporal lobe epilepsy, with the use of modern surgical equipment. There are data about performing radiofrequency (Parrent A.G., Blume W.T., 1999; Liscak R. et al., 2010) or laser (Willie J.T. et al., 2014, Grosse R.E. et al., 2016) thermoablation of amygdalohippocampal complex, with the use of the temporal or occipital stereotactic approaches.

From 1998 to 2010 at the clinic of the N.P. Bechtereva Institute of the Human Brain of the Russian Academy of Sciences (St. Petersburg) we have operated 21 patients with drug resistant temporal lobe epilepsy using two-stage stereotactic operations. The first stage included the implantation of the deep brain electrodes to record epileptic activity in uncus, amygdaleum and the hippocampus, with subsequent stereotactic ablation of the identified epileptogenic zones with the cryosurgical method, during the second stage of treatment. Lateralization of the operation was determined by the data set of EEG, MRI and fluoro-deoxyglucose PET. Surgery was performed using stereotactic temporal approach. The average total volume of ablation in mediobasal temporal region was 4.5–6 cm^3. Despite the fact that no one patient after surgery demonstrated neurological and psychological deterioration, the outcome of operations were rather unsatisfactory – the result IA class on the Engel scale was achieved in only 33.3% of patients. We concluded that the possible reasons were, first, insufficient correct selection of patients for surgery, and secondly, too small volume of destruction in the target points. A number of authors suggest that the entorhinal cortex and other adjacent to amygdalohippocampal complex structures also play the role in the epileptogenesis and spread of epileptic activity and so they have to be regarded as the stereotactic targets.

Given these considerations, in 2016, we resumed conducting stereotactic destructions in patients with temporal lobe epilepsy, using modern equipment for operations and 3 T MRI stereotactic localization of targets. We used the cryoprobe forming tissue destructions up to 6 cm^3 in each target point. 4 patients have been operated on, and destructions in the whole hippocampus and the uncus of parahippocampal gyrus were completed with the total amount of destruction about 12–18 cm^3. Destructions in the amygdaleum have not been conducted in this group of patients, because of the absence of epileptic activity in this structure, according to the registration with the deep brain electrode. One patient underwent a combined surgery with the resection of the pole of the temporal lobe and stereotactic cryodestruction of the hippocampus. We noted that the used probe working with the temperature of the solid carbon dioxide forms the foci of cryodestruction with standard sizes and shapes, with a clear demarcation that allowed us to carry out a thorough preoperative planning of stereotactic interventions.

To date, all the patients are free of seizures, with no complications occurred in the postoperative period. Thus, significant advantages of stereotactic surgery for temporal lobe epilepsy are the safety and best toleration by patients compared to open surgery. The use of new operating techniques allows to increase the therapeutic outcome of such interventions.

#8475

Stereo-EEG Implanted Electrodes with Neuronavigation Arm

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Keywords: Stereo-EEG, Epilpesy surgery, Neuronavigation.

Introduction and Objectives: The study of complex refractory epilepsies frequently requires data form invasive EEG. The regions of interest can be monitored with depth electrodes. These electrodes are usually implanted with stereotactic frames or robotized systems that are not readily available in many centres with a smaller surgery volume. Over the last years, neuronavigation has proven to be a valuable tool capable of replacing classic stereotactic frames in less precision demanding surgeries. In this work we analyse the precision of non-frame based system for the implantation of stereo-EEG (SEEG) electrodes in our centre.

Material and Methods: The retrospective analysis included all patients with medically refractory focal epilepsy who underwent implantation of depth electrodes for extraoperative EEG monitoring between June 2012 and January 2016. Trajectory planning was done with either Cranial™ 4 or Synergy Cranial™ 2.2 from Medtronic® and implantation of Dixi® or Alcis® electrodes was done with Mayfield® head clamp and Vertek® II articulated arm. All patients underwent early post-operative image control of implantation that was fused with pre-operative imaging. Analysis of demographics included entry-point and target accuracy, depth of each trajectory, procedure-related complications and quality of EEG recording.

Results: Fifty-one SEEG electrodes were implanted in 6 patients. Their mean age was 27.5 years (8–49 years old). On average, 8.25 electrodes were implanted per patient. The average time of implantation planning was 45 minutes. The average operative time was 141 minutes (range 104–178 minutes) with an average of 17 minutes per electrode (range 14.86–19.17 minutes). Measured accuracy obtained from entry point in 4 patients (35 electrodes) and target in 5 patients (45 electrodes) demonstrated a median entry point error of 2.41 mm and a median target point error of 2.51 mm. Planned target regions were reached in all 51 trajectories and there weren't any procedure-related complications. Seizures were detected in more than one electrode in all 6 patients and a strategy was possible to delineate with data obtained from this SEEG.

Four patients were further operated with focal resections (2 are in Engel I and 2 in Engel III), one was implanted with DBS in ANT with seizure severity improvement and one refused resective surgery.

Discussion and Conclusions: This technique of implantation of SEEG depth electrodes has the necessary accuracy to achieve the goals of this type of EEG monitoring. In spite of having a lower accuracy compared to the classic systems, knowing the error margin allows us to establish security boundaries in order to avoid vascular structures. The simpler workflow of the neuronavigated implantation of depth electrodes can make this kind of investigation readily available in more epilepsy centres, improving their ability to treat even more complex cases.

#8497

Epidural Empyema as a Late Complication of Complex Epilepsy Surgery

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Keywords: Epidural empyema, Epidural abscess, Epilepsy surgery, Skin erosion, Intracranial recordings, Complications.

Objectives: Presentation of an unusual case of a late intracranial infection in a patient with history of epilepsy surgery.

Methods: A 48 year old female patient with medically-resistant extratemporal epilepsy underwent two stages operation in 2012. In stage I, she underwent a left fronto-temporal craniotomy and subdural electrodes were placed over the left fronto-temporal cortical area. Following a week of intracranial recordings she underwent, stage II operation with left frontal multiple subpial transection (Morrell operation) and anterior 1/3 corpus callosotomy. She had an uneventful post-operative course and the epileptic activity was successfully controlled with anticonvulsive therapy. Recently, she presented with a swelling of her left frontal scalp, pyrexia (38.5 ºC), generalized weakness and memory deficits. Her brain CT scan revealed an epidural collection.

Results: She underwent surgical exploration in the operating theater. Skin necrosis adjacent to her old skin incision was noted. Following debridement of the necrotic areas a purulent subcutaneous collection was found and evacuated. The bone flap of the old craniotomy was removed and osteomyelitic foci were identified. The epidural space had an abundant collection of pus that was also evacuated. After meticulous irrigation and debridement, the dura matter remained intact. The bone flap was discarded and the skin sutured properly. Staphylococus hominis was cultivated from the wound. Antibiotic therapy with vancomycin and metronidazole was commenced, according to sensitivities. Post-operatively, the patient had 2 seizures that were successfully controlled with anticonvulsants. She remained afebrile after the 2nd week.

Conclusions: Skin erosion along old skin surgical incision and epidural empyema formation could be an uncommon late complication, following consecutive epilepsy operations. In our case, surgical debridement with empyema evacuation, craniectomy and antibiotic therapy, secured patient full recovery.

#8595

Intracranial Stimulation in Children with Refractory Epilepsy: A Case Series

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Keywords: Epilepsy, Cortical stimulation, Deep brain stimulation.

Objectives: A pilot study evaluating the efficacy of intracranial stimulation at treating medically refractory epielpsy in children.

Methods: A retrospective analysis of eight children who underwent intracranial electrical stimulation for the investigation

and treatment of their refractory epilepsy at King's College Hospital between 2014 and 2015. Five had subacute cortical stimulation (SCS) during intracranial video-telemetry with efficacy of stimulation evaluated by counting interictal discharges and seizures (both clinical and subclinical). Three other children underwent deep brain stimulaton (DBS) of the centromedian (two patients) or anterior (one patient) thalamic nuclei. The incidence of interictal discharges was evaluated visually and quantified automatically.

Results: Three patients had thalamic DBS (one with idiopathic generalized epilepsy, one with presumed symptomatic generalized epilepsy and one with right fronto-temporal epilepsy) and 5 patients had SCS (one with temporal lobe epilepsy and four with frontal lobe epilepsy). Among the three children with DBS, two had >60% improvement in seizure frequency and severity and one had no improvement. Among the five children undergoing SCS, four showed improvement in seizure frequency (>50%), severity of seizures and interictal epileptiform discharges (>75%) while one chid did not show improvement. Procedures were well tolerated by all children.

Conclusion: Cortical and thalamic stimulation appear to be effective and well tolerated in children with refractory epilepsy. Subacute cortical stimulation can be used to identify the focus and predict the effects of resective surgery. Further larger studies are necessary.

#8620

Surgical Treatment for Refractory Epilepsy: Volumetric Analysis of Hippocampal/ Amygdala Resection in MTLE and Case Series Review

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Introduction: There is considerable debate over the extension of mesial temporal structures needed for epilepsy control in MTLE. Outcomes have been reported in the literature that corresponds with very dissimilar resection lengths of hippocampus and amygdala resections. A few works have tried to relate hippocampal linear resection length to outcome and found no direct relation, but there are still no reports on high-filed MRI measured volume of resection of mesial structures and its relation with outcome.

Objectives:

1. To determine if the volume of hippocampal and amygdala resection in MTLE correlates with outcome, namely with seizure control and post-operative deficits.

2. To review the long term outcomes of a single center series of resective epilepsy surgery.

Methods: Resection volume determination was performed on pre and post-operative high resolution isotropic coronal T1 3 tesla MRI, using ITK-Snap software; MRI structures were segmented with 3 plane orthogonal verification, according to EADC-ADNI harmonized protocol for hippocampal segmentation volumes were then correlated with outcomes. For the surgical series review, a database was created with patient data and statistical analysis performed with SPSS.

Results: 1 – Volume measurements: Post-operative hippocampal volumes ranged from 722 to 2956 mm^3 and post-operative amygdala volumes ranged from 215 to 2600 mm^3. Worst post-operative seizure control correlated with larger post-operative hippocampal remnants while no differences were found with post-operative amygdala volumes.

2 – Case series: A total of 177 patients (50% male, 48.3% female) were included with a mean age of 39.24 years old. The main clinical manifestation was complex partial seizures (59.4%), with a mean value of 12.7 seizures/month. There is a prevalence of mesial temporal sclerosis epilepsy in 47.8% patients, extra temporal epilepsy being the second most frequent type of epilepsy. In this group 43.9% of patients were submitted to amygdalohippocampectomy with anterior temporal lobectomy, followed by lesionectomy in 36.7% of cases.

Better results were achieved in mesial temporal lobe epilepsy with 85% of patients in Engel 1 at 5 years follow up and worse results came from extra temporal epilepsy, in line with published literature.

Conclusions: Volume evaluation of mesial temporal lobe structures in MTLE can be a useful predictor of seizure control and be used as a relevant clinical tool, paving the way to tailored patient resections.

In our series, surgery resulted in good (extra temporal epilepsy) to excellent (MTLE) seizure control with minimal morbidity and no mortality. Further efforts should be developed to perform surgery for refractory epilepsy earlier in the course of the disease.

Experimental

#8037

Stereotactic Surgery Before Brain Surgery

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Keywords: History stereotaxy contremoulins.

A 1947 historical paper by American neurosurgeon Ernest Spiegel is reputedly the first description of human medical use of a stereotactic device, thirty years after Sir Victor Horsley and Robert Clarke employed it to create an animal brain atlas. Nevertheless, both the principles and application of stereotaxy date from the late XIXth century.

The invention and first surgical use of a stereotactic device are due to Gaston Contremoulins, a 26-year-old self-taught scientist who worked at the department of experimental physiology of Paris Medical University. The technique was published in 1897 in scientific and popular newspapers, which focused on two remarkable procedures of stereotaxy-assisted intracranial bullet removal.

We describe this original technique and the key concepts formulated through it, as well as the epistemological context of their

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birth. Surprisingly, the founding project of what proved to be a major advance in neurosurgery was not supported by conventional scientific institutions and it had to be crowdfunded, through non scientific media.

Despite the fast and massive spread of the technique in France (more than 37,780 patients benefited from intracranial or extracranial stereotactic procedures during World War I), its international diffusion in the scientific community was limited, and the potential developments of this revolutionary technique were not immediately explored.

This can be imputed to the lack of openness of medical academic institutions to a self-taught scientist, as well as the complex historical context.

This highlights how much cross-disciplinary research and creative culture are key for significant medical breakthrough.

#8477

Network-Level Effects of Deep Brain Stimulation: fMRI Study of Electrical Microstimulation in the Internal Segment of the Globus Pallidus in Monkeys

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Keywords: Deep brain stimulation, fMRI, Monkey.

Introduction: Deep brain stimulation (DBS) is an established therapy for various movement disorders (e.g Parkinson's disease, dystonia and essential tremor) and its further applications, especially in psychiatric diseases, is currently being explored. However, its underlying therapeutic mechanisms in the brain network remain largely unclear. Changes of cerebral blood flow in several regions of the cortex and the basal ganglia have been demonstrated with DBS using positron emission tomography (PET) or single photon emission computed tomography (SPECT) in some previous studies, but their results were not always consistent with each other. Here, we performed a functional magnetic resonance imaging (fMRI) experiment to further our understanding of the effect of electrical stimulation in the basal ganglia at the full brain scale.

Materials and Methods: Two male rhesus monkeys (*Macaca mulatta*) participated in this study. Prior to the experimental sessions, a head-post and a recording chamber were implanted under general anaesthesia. Then, in the fMRI sessions, we measured blood oxygen level-dependent (BOLD) effect at 3.0-Tesla with a single surface coil during electrical microstimulation in the internal segment of the globus pallidus (GPi) under light general anaesthesia. Before each MRI scanning, an MR-compatible bipolar stimulating electrode was inserted in the somatomotor region of the GPi. After verifying its position with a T1-weighted image, we acquired full brain EPIs (1.5 mm isotropic voxels, TR = 2.4 s) in a block design alternating 30 s of ON/OFF stimulation. We used two types of stimulation paradigm: 1) 120 Hz stimulation with various values of total electrical energy delivered (TEED), and 2) stimulation at three different frequencies (20, 120 and 260 Hz) with constant TEED.

Results: The 120 Hz stimulation of the somatomotor region of the GPi significantly increased the BOLD signal in several areas in the cortex and subcortical structures. Regarding the cortex, activations were seen in a lateral part on both sides of the central sulcus, the primary motor and sensory cortices, not only in the ipsilateral hemisphere but also in the contralateral hemisphere. In the subcortical structures, the GPi stimulation led to activations in the ventrolateral nucleus of the thalamus and subthalamic nucleus ipsilaterally. Moreover, we found increased activation in the contralateral cerebellar cortex. In most of these activated areas, the more TEED was delivered, the larger change of the BOLD signal was produced by the 120 Hz stimulation. On the other hand, there was an obvious effect of stimulation frequency; in spite of the same TEED, maximal increase in BOLD signal was observed at the 120 Hz stimulation, and less activations were induced by the 20 and 260 Hz stimulations.

At the same time, the GPi stimulation induced deactivations in some areas in the temporal and parietal cortices, but there was no clear frequency-dependent effect on the deactivations.

Conclusions: Our study has revealed significant increase in BOLD effect in several areas of the cortico – basal ganglia – thalamic loop and cerebellum during electrical stimulation in the somatomotor area of the GPi. This effect was stimulus frequency-dependent, showing stronger influence at 120 Hz. This is consistent with the clinical observation on patients with DBS in which stimulation at 100–200 Hz is the most effective.

#8502

Internal Pulse Generator in Deep Brain Stimulation: Rechargeable or Not?

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Keywords: Deep brain stimulation, Cost-effective analysis, Hardware-related complications, Internal pulse generator, Rechargeable battery.

Objective: Deep Brain Stimulation (DBS) is a cost-effective strategy for the treatment of different neurologic disorders. Hovewer, DBS procedures are associated with high costs of implantation and replacement of the internal pulse generator (IPG). Different manufacturers propose the use of rechargeable IPGs. The objective of this study is to compare the implantation costs of non-rechargeable IPGs versus the estimated costs of rechargeable IPGs in different categories of patients to evaluate if an economic advantage for the health care system could be derived.

Methods: The study looked at 149 patients who underwent a surgical procedure for IPG replacement. In a hypothetical scenario, rechargeable IPGs were implanted instead of non-rechargeable IPGs at the time of DBS system implantation. Another scenario was outlined in a perspective period of time, corresponding to the patients' life expectancy. Costs were calculated, and inferential analysis was performed.

Results: A savings of 234,194 euros, including the cost of management of complications, was calculated during a follow-up period of 7.9 years. In a comprehensive life expectancy period of 47 years, a savings of 5,918,188 euros would be obtained ($P < 0.05$). Long-terrm group data point out that a relevant savings would be expected from implantation of rechargeable IPGs in dystonic patients ($P < 0.05$) and in patients with Parkinson disease ($P < 0.05$), and a savings is projected to occur in other categories of patients ($P < 0.05$).

Conclusions: Implantation of rechargeable IPGs presents clinical advantages compared with non-rechargeable devices. A huge economic savings can be realized with the implantation of rechargeable IPGs in categories of patients implanted with IPGs for DBS.

#8507

Long-Term Motor Deficits after Controlled Cortical Impact in Rats Can Be Detected by Fine Motor Skill Tests But Not by Automated Gait Analysis

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Keywords: Traumatic brain injury, Controlled cortical impact, Forelimb impairment, Behavior.

Animal models with constant, long-lasting motor deficits together with the right tests to assess behavioral abnormalities are needed to study the effectiveness of potential therapies to restore motor functions. In the current study, controlled cortical impact (CCI) was applied in rats to induce damage to the forelimb area of the motor cortex and the dorsal striatum. Motor behavior was assessed before and after CCI using fine motor skill tests such as the adhesive removal test, the cylinder test and the Montoya staircase test as well as the automated gait analysis system CatWalk XT over a 6 week period.

CCI caused a variety of unilateral motor deficits, which were characterized in detail by using various fine motor skill tests. Neither forelimb impairments, nor general changes in gait were detected with the CatWalk XT.

In this paper, we present both the methodology to induce long-lasting forelimb impairments as well as a comprehensive evaluation of which behavioral tests are suitable to measure unilateral motor deficits in rats after CCI.

#8518

Effects of 5 Weeks Fornix Deep Brain Stimulation in a Transgenic Alzheimer Rat Model

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Keywords: Fornix, Deep brain stimulation, Alzheimer's disease, Memory.

Background: Deep brain stimulation (DBS) is promising therapy in patients with Alzheimer's disease (AD). Few studies have suggested that stimulation of the forniceal area might slow down the cognitive decline of AD patients, but its biological effects on memory circuits remain unclear.

Objective: To study the behavioral and histological effects of continuous chronic DBS of the fornix in a transgenic Alzheimer murine model and wild type (WT) rats.

Methods: We used a transgenic Alzheimer rat model TgF344-AD that manifests age-dependent cerebral amyloidosis, taupathy, gliosis and apoptotic loss of neurons in the cerebral cortex and hippocampus, as well as cognitive disturbance. All the 18 month-old rats were surgically implanted in stereotactic conditions, using a portable microstimulator for chronic DBS in freely moving rats, allowing a chronic continuous stimulation for 5 weeks. Cognitive tests (open field and Novel Object recognition test) were performed before surgery, and after 2 and 5 weeks. At 5 weeks the animals were sacrificed for immunohistochemical study. Implanted but non stimulated rats were used as controls.

Results: We confirmed the above described differences between transgenic AD rats not stimulated and WT rats not stimulated. Moreover we found that DBS in the transgenic rat model led to a significantly reduce in ABeta deposition: 30% +- 12% $p < 0.001$; decrease neuroinflammation markers (using Iba1 and GFAP antibodies): 150%/50% ($p < 0.001$) respectively as compared to non stimulated rats. DBS in the transgenic rat model prevented neuronal loss (with NeuN immunostaining) and synaptic (Synaptophysin staining) loss $p < 0.001$. Cognitive tests suggested an improvement of memory in the DBS transgenic rat model but did not differ significantly between groups.

Conclusion: In the Tg-F344-AD rat model, 5 weeks of forniceal DBS decreased amyloidosis and inflammatory responses, prevented neuronal and synaptic loss in the cortex and hippocampus. These findings show a neuroprotective effect of forniceal DBS in this transgenic Alzheimer rat model.

#8596

Visualization of the Cerebrovascular Glycocalyx

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Keywords: Blood-brain barrier, Glycocalyx.

Introduction: The glycocalyx is a gel-like layer lining the luminal surface of the endothelium. The glycocalyx exerts an important barrier role because it prevents exposure of plasma cells and components to the endothelial surface. Disruption of the glycocalyx by local inflammation or ischemia results in decreased glycocalyx thickness which is associated with a number of vascular diseases and reduced endothelial barrier function. The cerebrovascular glycocalyx has sparsely been studied. Because of its important barrier properties we consider the glycocalyx as a part of the blood-brain barrier. Therefore, the glycocalyx may have a potential role in cerebrovascular disease.

Methods: Visualization of the cerebrovascular glycocalyx is best performed in a clinical setting because of significant collapse in *ex vivo* microscopy. Using Sidestream Darkfield (SDF) imaging we have recorded sublingual and cerebral glycocalyx dimensions during surgery for cerebral oncology surgery and epilepsy surgery. This technique can be performed clinically and is based on estimation of the 'red blood cell column' exclusion zone. From this, the perfused boundary region (PBR) can be calculated by GlycoCheck © software. The PBR is an established indirect gauge of the glycocalyx and expressed in micrometers (μm) per vessel diameter. The local medical ethical committee has approved this study.

Results: First, sublingual glycocalyx dimensions were determined. Next, we have visualized the cerebral microcirculation using SDF imaging. We were able to establish the dimensions of the cerebrovascular glycocalyx. Our protocol and results will be presented by using illustrative images and video fragments of SDF imaging. Glycocalyx dimensions are shown in a table to compare between sublingual and cerebral dimensions.

Discussion: In this study we were able to visualize the cerebrovascular glycocalyx in a clinical setting. Also, we have illustrated that imaging of the cerebrovascular glycocalyx by SDF imaging is safe, quick and easily performed. Evaluation of the glycocalyx in specific cerebrovascular diseases in which a disrupted blood-brain barrier has been suggested, like epilepsy and stroke, can now be performed. Thus, a potential role of the glycocalyx in blood-brain barrier function can be assessed using this technique.

#8821

Cone-Beam-CT in DBS Surgery

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Keywords: Deep brain stimulation, Cone-beam-CT, Perioperative CT, Stereotaxy.

Objective: To report the findings of our research for optimizing the logistics perioperative deep brain stimulation (DBS) surgeries using a cone-beam-CT (CBCT) scanner available in our hybrid operating theatre.

Methods: We fixated a Leksell stereotactic frame (Elekta, Sweden) on a phantom skull with the CT indicator and placed it in the CBCT (Allura Xper FD20, Philips, the Netherlands). We used the same phantom to make a 'normal' CT-scan (Somatom Force, Siemens, Germany). Both scans were uploaded in the Framelink software (Medtronic, USA) for the fusion.

Results: We successfully and accurately fused the stereotactic CBCT with a normal CT using the Medtronic Framelink software.

Conclusion: In our experience CBCT can be a useful imaging method for stereotaxy in DBS surgeries and might play an important role as a preoperative and postoperative stereotactic scan. Futher research is needed with CBCT and MRI fusion.

Movement Disorders

#8160

DBS for NBIA-Related General Dystonia. Eight Years Follow-Up

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Keywords: NBIA, DBS, Dystonia.

Conservative and surgical treatment of Neurodegeneration with Brain Iron Accumulation (NBIA) is difficult and frequently ineffective. The authors present a group of patients with clinically

and radiologically diagnosed NBIA with genetically confirmed PANK2 mutation, treated with deep brain stimulation.

Materials and Methods: Twelve patients with confirmed PANK2 mutation (NBIA-PKAN) were treated with deep brain stimulation between 2008 and 2015. Age of the patients varied from 8 to 24 years. The clinical condition of the patients was evaluated with scales and video recorded. At all cases the permanent electrodes were implanted to the subthalamic nuclei or globus pallidus. 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 noted among the group. Caregivers of the patients noted subjective improvement of the clinical state of the subjects that was confirmed with tailored scales. More significant improvement was noted among STN group compared to GPi group.

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

#8423

The Use of Dexmedetomidine during Deep Brain Stimulation for Tourette Syndrome: A Case Report

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Keywords: Deep brain stimulation, Tourette syndrome, Dexmedetomidine.

Introduction: Deep brain stimulation is effective in reducing the key symptoms in selected cases of severe Tourette syndrome. The surgical approach can be challenging due to the presence of severe tics. Often the patients are operated on with local anesthetics and conscious sedation. However, there is no 'gold standard' for anesthetics which should be used. The goal of anesthesia should be to achieve conscious sedation to suppress the tics as much as possible but to allow for intraoperative testing. In addition, anesthesia should not interfere substantially with neurophysiological measurements. Here, we describe a case report in which dexmedetomidine is used in a patient with Tourette syndrome and discuss the advantages of this drug as anesthetic for awake deep brain stimulation procedures in Tourette syndrome.

Case Description: This 19 year old male developed tics around the age of eight. Tics started with simple motor tics like head shaking, but later they extended to the rest of his body. They became more severe during childhood and adolescence. He suffered from severe and almost continuously present motor tics like eye blinking, head shaking and jerks of shoulders, arms, abdomen and legs and he had mild vocal tics like sniffing and coughing. First and second line medication treatment and behavioural therapy were not effective in the past.

The patient was scheduled for deep brain stimulation. An awake approach with local anesthetics and continuous infusion of dexmedetomidine 0.5 mcg/kg/u was used. Bilateral electrodes were placed in the globus pallidus internus. During the procedure, tics were suppressed adequately, the patient was conscious and no evident interference was observed with micro-electrode-recordings. It was clearly possible to record globus pallidus externus and internus neuronal activity and no activity was found at the level of the laminae. No perioperative adverse events occurred.

Conclusion: The used anesthetic, Dexmedetomidine, an α2-agonist, is a sedation agent which can be used in deep brain stimulation surgeries for patients with Tourette syndrome due to a favorable mechanism of action. Dexmedetomidine has sedative and analgesic properties without inducing respiratory depression. It mimics a sleeping sensation in which patients are easily arousable allowing appropriate clinical testing. Importantly, there is a dose dependent suppression of tics. Compared to other sedative agents such as propofol, benzodiazepines and volatile agents, dexmedetomidine does not activate the gamma-aminobutyric acid (GABA) receptors. Activation of GABA, the major inhibitory neurotransmitter within the basal ganglia, can worsen or abolish micro electrode recordings.

#8450

Evaluation of Neuroprotective Effect of DBS STN: Long Term Clinical Studies Review

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Keywords: Neuroprotection, Deep brain stimulation, Parkinson disease.

High frequency chronic deep brain stimulation of subthalamic nucleus (DBS STN) has become a routine method for the treatment of advanced PD, leading to striking improvements in motor function and quality of life of patients. The subthalamic nucleus is a key node in the functional control of motor activity in the basal ganglia. The dopamine loss that occurs in PD augments STN activity and its inhibition, by for example DBS, suppresses the motor signs in human patients, together with animal models of Parkinson's disease.

It is hypothesized that this augmented STN activity in turn, may cause further damage to the vulnerable dopaminergic neurons; glutamate output from STN to the substantia nigra contributes to the neurotoxic process underlying dopaminergic cell death in Parkinson's disease, thereby creating a scenario for an ongoing cycle of neuronal loss in the SNc The inhibition of STN neurons by DBS may result in the suppression of their glutamate output, and hence lessen the nigral cell death. In addition, there is also evidence that

high-frequency activation of glutamatergic synapses triggers the release of BDNF, a protein brain-derived neurotrophic factor capable of protecting neurons from degeneration. Here we review the clinical evidence of neuroprotection secondary to DBS STN.

Methods: We will consider only the long term evaluation studies (>4 years) that have also a proper off medication/off stim evaluation. The systematic review identified 12 studies that cover the set criteria. All clinical trials reported symptomatic positive results, even when compare with best medical therapy, but did not precisely address the neuroprotection.

Results: The study by Merola et al is the only one that has investigated the comparative potential disease modifying effect of DBS STN vs. best medical therapy. They found a comparable pattern of progression of motor scores and cognitive/behavioral alterations in treated and non-treated groups with no reduction of the motor scores during off medication/off stimulation evaluation59]. In general, in all the other 'neuroprotection' studies, evaluation during off stimulation/off medication after >4 years did not show disease modifying effects when considering motor scores. In fact, Zibetti, Gervais-Bernard found a worsening of motor scores (7%) after 5 year of follow up and Visser-Vandewalle reported a 26% (albeit not significant) worsening after 4 years. The remaining studies found stable motor score or non-significant improvement after >4 years post DBS STN. One key short term study, addressing the issue of disease modification specifically, was by Hilker. In a prospective two center study, disease progression was determined by means of serial 18F-fluorodopa (F-dopa) positron emission tomography (PET) in 30 patients with successful STN DBS over the first 16 (SD 6) months after surgery. The results suggested an annual progression rates relative to baseline of 9.5–12.4% in the caudate and 10.7–12.9% in the putamen, within the range of previously reported data from longitudinal imaging studies in PD.

Conclusion: Unlike many experimental, preclinical examples, evaluation of DBS STN neuroprotection has proven problematic in the clinical situation. We are very much limited by the clinical measures that are currently at our disposable. Up until an accurate measure of neuroprotection can be found clinically, we are left with the situation of any potential neuroprotective effects being masked and entangled by the 'symptomatic effects' of DBS STN.

Keywords: Neuroprotection, Deep brain stimulation, Parkinson disease, Long term clinical studies.

#8455

Hypnosis for Awake Bilateral DBS (Deep Brain Stimulation) of Gpi in a Young Woman with Secondary Dystonia

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Keywords: Dystonia, DBS, Gpi, Hypnosis, Secondary dystonia, Infantile cerebral palsy.

Background: Hypnosis can be described as a highly focused, absorbed attentional state that minimises competing thoughts and sensations. Hypnotic suggestibility is normally distributed in human populations and remains a stable individual trait. It is heritable as shown in classic twin studies. The genotype Val/Met variant of the Catechol-O-Metyltransferase (COMT) gene is more frequent in individuals with high hypnotic suggestibility. Interestingly, it is associated with prefrontal executive functions and working memory. Several neuroimaging studies have brought to light the neural basis of the hypnotic experience. Used as anesthetic since the early 1800's (first reported surgery in 1829), it was almost abandoned with the introduction of chemical anaesthesia. In recent years its application gained interest in neurosurgery.

Awake craniotomy with intraoperative neurophysiological monitoring is the emerging application field of hypnosis technique as a reliable method to control pain and discomfort during cortical and subcortical mapping of motor and language areas. A new promising field of interest of this technique is the DBS surgery, to avoid discomfort and enhance the reliability in detecting side effect during microstimulation in patients affected by PD and dystonia. Fully awaken procedures are proposed to young adult patients affected by dystonia in our center but not always accepted. Hypnosis may be the effecting and safe option in this cases. Difficulties in copying with the stress are often the only limitation to this method.

Objective: To describe a method for awake DBS surgery based on hypnosis.

Methods: We started proposing hypnosedation procedure to patients undergoing awake surgery for DBS from January 2015. One patient was enrolled: a 26 years-old woman affected by secondary dystonia due to ICP (pre-operative BFMDRS-M: 76/120). A tailored induction was performed, leading the patient to her safe place, giving different suggestions according with the sensations elicited by the surgery and considering the preferences of the patient. The patient underwent a bilateral DBS of Gpi with intraoperative microrecording and stimulation.

Results: The DBS conducted in hypnosis condition was successful. Burr hole and injection of anaesthetics were the procedures reported as unpleasant. During surgery, we were able to detect side effect, in particular visual disturbances, during microstimulation through different trajectories without discomfort or fear of our young patient. One year after DBS of bilateral Gpi with

standard parameters, the improvement of dystonia was remarkable (post-op BFMDRS-M: 53/120; more important improvements were detected on mouth, speech, neck and trunk items).

Conclusion: The main findings are the effectiveness and reliability of the technique in performing DBS, the efficacy of hypnosis to reduce dystonic movements until a complete temporary resolution, and the positive psychological impact of the technique on this dystonic patient submitted to DBS.

#8460

DIRECT DBS: A Prospective, Multi-Center Clinical Trial with Blinding for a Directional DBS Lead

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Keywords: Deep brain stimulation, DBS, Subthalamic nucleus, STN, STN-DBS, Parkinson's disease, Directional DBS, Neurostimulation, Randomized, RCT.

Introduction: Historically, DBS systems have delivered stimulation using cylindrical electrodes, which stimulate neurons around the entire circumference of the lead. In this study, we will test a directional DBS lead, which includes radially segmented electrodes designed for selective stimulation in directions orthogonal to the lead trajectory, in addition to standard cylindrical electrodes. Bilateral directional DBS leads will be connected to the Boston Scientific Vercise PC pulse generator, which provides an independent current source for each of its 16 contacts. This system, therefore, is capable of current steering to shape stimulation in the plane orthogonal to the long axis of the lead (directional stimulation), as well as providing Ring Mode (omnidirectional) stimulation equivalent to historical leads. We aim to characterize the effects of directional stimulation in subjects implanted with this system.

Methods: Direct Dbs is a prospective, randomized, multicenter, double-blind study employing a crossover design. Subjects (N = 10 to 12, adaptive) will be enrolled per center standard of care and implanted with a directional lead (Cartesia, Boston Scientific) included as part of a directional Vercise PC system for bilateral STN-DBS. Study visits occur in 3 major periods– during implant, at 3 months, and at 1 year. Programming is restricted during the first 3 months post-implant to Ring Mode. At 3 months, multiple single-day programming visits will be undertaken to optimize directional programming. Patients are then randomized to one of two arms (4 weeks per arm) for a double-blind crossover comparison between Ring Mode and unrestricted (e.g. directional) programming. After the crossover phase, subjects enter an open-label phase of the study, with follow-up at 1 year.

Results: This exploratory study will have no prospective statistical hypothesis, but will collect data such as side effect threshold, therapeutic window, UPDRS scores, and quantitative accelerometer-based measures of bradykinesia and tremor.

Discussion: DIRECT DBS is an exploratory study which will investigate the effects of subthalamic deep brain stimulation (DBS) using directional DBS leads with current steering in patients with Parkinson's disease. The DIRECT DBS trial will compare the effects of directional stimulation and omnidirectional stimulation over the first year post-implant. Results will inform future studies.

#8484

Electrophysiological Findings during DBS as a Salvage Bilateral Procedure Two Years after Initial Successful Unilateral Gamma Knife Thalamotomy for Essential Tremor

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Keywords: Thalamotomy, Deep brain stimulation, Gamma Knife, Tremor, Ventro-intermediate nucleus.

A 71-year-old male has been diagnosed with drug-resistant essential tremor (ET), in a familial context, with symptoms that started in childhood, at the age of 11. Tremor was predominant in the right upper limb, in a right-handed patient, provoking dramatic functional impairment.

Due to a relative contra-indication to DBS (anticoagulation treatment for pulmonary embolism), an initial Gamma Knife (GK) thalamotomy of the left ventro-intermediate nucleus (Vim) was performed. After progressive and dramatic clinical alleviation, which persisted up to two years, the tremor relapsed. Magnetic resonance imaging (MRI) showed the presence of a small contrast-enhancement (CE) surrounding a hypodense T1 necrotic core which, after co-registration with the dosimetry palnning in the Leksell GammaPlan, corresponded to the GK targeting. Additionally, the DWI data made possible the semi-automated segmentation of 7 clusters of thalamic nuclei, with the ventro-lateral ventral (VLV, nomenclature as from Morel et al.) cluster containing the contrast-enhancement area, as corresponding to the GKS target and in a ventral position, having anatomical relevance.

A deep-brain stimulation (DBS) procedure was decided after multidisciplinary discussion. Due to the fact that the patient had

bilateral tremor, and DBS could offer bilateral implantation without additional risks, it has been decided to treat both sides. For the left previously treated by GK, we aimed at stimulating the vicinity of the preexisting lesion. On this side, intraoperative microrecording showed that the center of the CE visualized lesion on MRI was silent (with no cells) and was surrounded by an area of normally active neurons; however, there was a clear difference in terms of potentials of action between the left (with previous GK) and the right (with no previous GK), raising the question whether new or surviving cells were present on the left. Additional data while comparing left and right tracks showed that neuronal noise, single unit amplitude and frequency were significantly higher on the non-GK treated side, suggesting that the cells on the previously treated left GK side were surviving and not new ones, different than those on the right. The patient had immediate and complete clinical alleviation after DBS.

However, three days after the DBS procedure, he presented with dysarthria and left hemisyndrome. A CT scan and angio-CT showed right sylvian hypoperfusion, with right carotid artery thrombus. An MRI performed at 1.5T revealed an ischemia on the territory of the right anterior choroidal artery and progression of the carotid thrombus. The patient has been putted under anticoagulation treatment, with further disappearance of symptoms. Additionally, tremor on the left side remained suppressed after the stroke, with no need for stimulation on that specific side. Eighteen months latter, this important alleviation persisted bilaterally, by unilateral stimulation.

Electrophysiological findings suggest functional reorganization at the periphery of the necrotic core visualized on the follow-up MRI after GK. Consequently, this peripheral area containing neuronal activity is most probably the one responding to DBS, although the former is not identhical on both sides, but with a final identhical clinical efect. Deep-brain stimulation after GK thalamotomy, aiming at a target closed to the previous lesion is possible and can lead to tremor suppression with durable effect. The analysis of the electrophysiological findings in this unique case helps to better understand the functional neuronal reorganization after GK thalamotomy.

#8493

Unilateral VIM and GPI Stimulation for Treatment of Holmes' Tremor Caused by an Arteriovenous Malformation in the Midbrain

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Keywords: VIM, GPI, Holmes' tremor.

Introduction: Holmes' tremor (HT) combines resting, postural and action tremor. The two treatment options are pharmacotherapy and deep brain stimulation (DBS). Pharmacotherapy is usually insufficient. The best surgical target is the ventral intermediate thalamic nucleus (VIM). In the absence of a satisfactory response or if the effects of stimulation diminish with time, alternative targets exist. We report on a young patient with HT who underwent unilateral VIM and globus pallidum internus (GPI) stimulation.

Case Report: In 2012, a 26 years old male patient known for a midbrain arteriovenous malformation (AVM) was diagnosed with HT. The AVM had been treated by embolization and radiosurgery in 2001. A second haemorrhage in 2009 resulted in left hemiparesis including the lower face, left internuclear ophtalmoplegia, and dysarthria. HT thus developed three years later, beginning in the left arm, and progressed to the rest of the left side of the body except the head. Brain magnetic resonance imaging (MRI) in 2012 showed traces of the haematoma located strictly on the right side in the mesencephalon including the area containing the central tegmental tract, as well as the lower thalamus, and bilateral hypertrophic olivary degeneration in the medulla oblangata. After failure of pharmacotherapy, the patient underwent DBS of the right VIM. The initial significant improvement of HT worsened after three months of stability, despite multiple stimulation adjustments. Nine months after the initial implantation, we added DBS of the right GPI which re-established therapeutic efficiency without side effects. This effect was stable at last follow-up (30 months), and the patient was neurologically autonomous.

Conclusion: VIM stimulation alone is an affective treatment to decrease various types of tremor. The complex physiopathology of HT, however, certainly involves dysfunction of at least two different systems: the dopaminergic nigrostriatal and cerebellothalamic pathways. Simultaneous stimulation of VIM and GPI for HT has previously been reported as successful; results of additional stimulation of the ventralis oralis anterior nucleus (VOA) are mixed. The present case confirms that targeting of two areas of the brain may be necessary: VIM stimulation proved insufficient but subsequent GPI stimulation resulted in significant lonf term improvement of HT.

#8503

Efficacy of Directional Leads in DBS for Movement Disorders

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Keywords: Directional leads, DBS, Movement disorders.

The efficacy of DBS in basal ganglia depends upon the effective stimulation of target nuclei: moreover, it results from a careful anatomical reperage, a sure intraoperative neurophysiology and a conscientious postoperative reglage. Light errors in surgical positioning, individual anatomy and variables in local electrical fields may decrease the efficacy of DBS. Tayloring the electric field may overcome some of these constrains. Recently, the main Companies involved in DBS technology developed directional leads, able to configure anisotropical electric fields, as to cover variable tissue volumes, according to clinical evidence.

The aim of this investigation is to verify the efficacy of directional leads in patients undergoing DBS for movement disorders.

10 patients (6M-4F, mean age 52 – mean disease duration 9 yrs) suffering from movement disorders (8 PD, 1 Generalized dystonia, 1 cerebellar tremor), underwent DBS (7 Stn, 2 Gpi, 1 RaPl) with stereotactic approach, obtained after anatomical reperage in volumetric Mri – normalized upon S&W atlas – with the aid of intraoperative MERs; three exploring traces were performed in mean on each side and the stimulating directional leads were positionedafter confirmation from semi-microstimulation along the best trace. Intraoperative evidence of the correct electrodes' positioning and orientation was obtained by means of plain fluoroscopy. Pre and postoperative clinical evaluation followed validated scores (UPDRS – BFMDRS – TRS). Mean FU is 6 months: for each patient were considered: clinical outcome, stimulus parameters, electrode configurations and orientation and possible adverse events.

9 patients are actually on FU; 1 drop out for infection of the IPG. Active leads are 17 as a whole; 15 leads in directional configuration and 2 in 'ring' configuration; in all the cases DBS is performed with monopolar stimulation; current is delivered through two directional contacts, with total current splitted respectively 25% and 75%, PW 60 microsec, Fr 130 Hz; mean delivered current is 2.3 mA, mean voltage is 2.2 V. The final configurations resulted after many sessions of reglage, during which the activation of the directional contacts obtained better clinical results than the activation in 'ring' mode. Last FU reported decrease of UPDRS III 50%, UPDRS II 70%, BFMDRS 60%, TRS 85%. Mean LEDD decrease was 50%. No collateral effects were recorded.

In conclusion, directional leads allowed us to obtain taylored electric fields in 15 sides out of 17, suggesting clinical effects more consistent than in 'ring' mode. No significant collateral effects were observed. Moreover, larger cohort of patients and longer FU are necessary to confirm these preliminary data.

#8506

What are the Side Effects of Deep Brain Stimulation in the Treatment of Parkinson Disease? A Single Center Experiences with 62 Patients

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Keywords: Deep brain stimulation, Parkinson disease, Complications.

Deep brain stimulation (DBS) is now widely used in the treatment of Parkinson's disease, tremor, and dystonia. In Parkinson's disease, recent work has demonstrated that early DBS may have a significant benefit on quality of life and motor symptoms while permitting a decrease in levodopa equivalent dosage. DBS is usually preferred in Parkinsonian patients who initially benefit from dopaminergic treatment and lose its effectiveness during disease progress. In this study, we retrospectively evaluated DBS side effects in patients with Parkinson disease.

62 Idiopathic Parkinson patients treated with DBS and followed during 2008–2014 were involved in our study. Four Condition Test was used in the in the assessment of treatment response, stimulus related side effects and the effect of DBS on symptoms during off medication/on DBS, on medication/on DBS, off medication/off DBS, on medication/off DBS. During follow-up, therapeutic and electrode impedance was controlled and parameters effective in symptom control and side effects were noted. When no pathology was detected, reimaging with cranial MR and CT was performed to define if there was a pathology on the localization of DBS target.

30 patients were women and 32 of them were men. Subthalamic nucleus was the target in 49 patients, globus pallidus internus was in 11 and ventrointermedial nucleus of thalamus was the target of DBS in 2 patients. Complications related to surgery, instrumentation and stimulation were defined.

With the results of our study, we want to share common complications of DBS during Parkinsonian patients follow-up. Clinicians should take care of these complications for the benefit of patients.

#8509

Treatment of Dystonia after Kernicterus with Deep Brain Stimulation. Validation of Clinical Benefits during Complicated Postsurgical Follow-Up

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Keywords: Dystonia, Deep brain stimulation, Kernicterus.

Introduction: Bilirubin-induced neurological damage (BIND, kernicterus) is today a rare cause of dyskinetic cerebral palsy due to aggressive treatment of perinatal hyperbilirubinemia. Neurological sequelae include extrapyramidal movement disorder, sensorineural hearing loss and impaired upward gaze. Surgical treatment of the dystonic-dyskinetic movement disorder has been reported successful with a high degree of variability.

Patient and Methods: An 11-year-old patient suffering from dyskinetic cerebral palsy was treated with deep brain stimulation (DBS) surgery using multiple array microelectrode recording for the placement of bilateral four-contact electrodes in the GPi. During the placement of the right DBS electrode a slight anterior deviation of the electrode tip was observed in the lateral fluoroscopy. Postoperative MRI showed an anterolateral deviation of the right electrode into the GPe. The right DBS stimulation could not be activated due to side effects. The right electrode was repositioned through a rigid insertion cannula eleven months after first surgery without the use of microelectrode recording. Four months of clinical follow-up are available for the assessment of clinical benefit and side effects of bilateral DBS therapy.

Results: After repositioning of the electrode the patient shows minor but steady clinical improvement. However, stimulation induced side effects with acute or delayed onset lead to repeated reprogramming of the stimulator. Normalization of body weight and minor improvements of activities of daily living are the most apparent clinical improvements so far.

Conclusion: Effects of DBS surgery for secondary dystonia are less pronounced and predictable than for the treatment of primary dystonia. In this case frequent clinical evaluation for the presence of therapeutic effects and side effects warrants slow but continuous progress in clinical response. However, relevant therapeutic effects in these patients are often not properly represented in the scaling systems of dystonia rating.

#8514

Infections in Deep Brain Stimulation: Shaving versus Not Shaving

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Keywords: Deep brain stimulation, Infection, Shaving, Complication.

Objective: To report our experience of infections in deep brain stimulation (DBS) surgeries comparing shaving versus no shaving of cranial hair. Non shaving is strongly preferred by the patients due to aesthetic and psychological factors.

Methods: This study is a prospective follow-up of the infection rate in 38 non-shaven DBS cases between July 2014 and December 2015 compared to our former infection rate with shaving in our center. Minimum follow-up was six months. All patients, except four epilepsy patients, recieved implantation of the electrodes together with de leads and internal pulsgenator (iPG) at one and the same session.

Results: In 39 non-shaven patients a total of 75 electrodes were implanted or revised with a mean follow-up of 15.5 months. One patient (2.56%) developed an infection of the implanted DBS-hardware.

Conclusion: In our experience not shaving in DBS surgery does not lead to more infections when compared to shaving.

#8521

Perioperative Technical Complications in Deep Brain Stimulation Surgeries

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Keywords: Technical, Complications, DBS.

Deep brain stimulation (DBS) surgeries are multi-faceted and the various steps are interconnected. This process has proven to be dynamic over time. Since its first implementation, the method of DBS surgery has undergone changes. Some key technical changes were three-dimensional (3D) neuroimaging modalities, high-gain amplification of electrophysiological signals, and advanced programming possibilities. The authors have performed hundreds of cases (>900 DBS surgeries) in seventeen years. Since then, we have encountered many expected and unexpected, specific and

general technical problems. Some of these technical problems were related to the stereotactic frame, stereotactic localizer and planning station. In this study, we describe the technical problems of DBS surgeries in detail and share our experience with these complications and their management for groups who are willing to start a DBS program or who have recently started.

#8527

Stereotactic Accuracy: A Systematic Review and Meta-Analysis

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Keywords: Accuracy, Frameless stereotaxy, Robot, Stereotactic frame, Stereotactic neurosurgery.

Objective: To compare reported accuracies of stereotactic frames, frameless systems and neurosurgical robot arms and the methodology by which the accuracy is measured. The main sources of error that are of effect on stereotactic accuracy were determined.

Methods: The databases of PubMed, Cochrane library and Google Scholar were consulted to identify studies containing data on stereotactic accuracy. Included were phantom or clinical studies on brain biopsy, DBS or SEEG procedures that reported data on application accuracy.

Results: 23 studies published between 1993 and 2014 were included for this review of which 20 studies were used in the meta-analysis. The total number of patients was 826 together with 8 phantom units, this adds up to a corresponding number of 6943 lead placements. Results were grouped according to the stereotactic method used in the categories frame-based, frameless and robot. Average accuracies were respectively: 1.62 (95% CI, 1.24–2.00), 2.21 (95% CI, 1.93–2.50) and 1.28 (95% CI, 0.80–1.77). Overall accuracy varied was 1.87 (95% CI, 1.66–2.07). Grouped by study design the average clinical accuracy is 2.05 (95% CI, 1.80–2.30) and phantom accuracy 1.68 (95% CI, 1.45–1.91).

Conclusion: Due to heterogeneityin measurement methodology it is hard to compare application accuracy between studies or systems. In order to compare results between studies it is important to establish a valid endpoint, for which recommendations are provided in this study.

#8530

Bilateral STN DBS in PD Patients with Camptocormia

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Keywords: Camptocormia, Deep brain stimulation (DBS), Parkinson's disease (PD), Subthalamic nucleus (STN), Globus pallidus internus (GPi).

Objective: Camptocormia is a disabling syndrome characterized by forward flexion that can be an idiopathic condition or associated with numerous diseases like movement disorders, especially Parkinson's disease (PD). Treatment options are usually futile and L-dopa shows little or no effect, contrary to some individual reports which indicate that some degree of improvement in posture could be expected in bilateral deep brain stimulation (DBS) of the globus pallidus internus (GPi) or subthalamic nucleus (STN) in PD patients with camptocormia. Outcome results are inconsistent, especially for STN and data is scarce. The objective of this article is to determine the efficacy of bilateral STN DBS in alleviating the degree of camptocormia in PD patients. Results and outcome of two PD patients with camptocormia who underwent bilateral STN DBS are presented.

Patients and Methods: A 67 year old female and a 66 year old male, both suffering from PD in the last 15 and 8 years, respectively, were subjected to bilateral STN DBS procedure. The positions of electrodes were verified with a postoperative magnetic resonance imaging. The results were objectivized by measuring thoracolumbar flexion angle before and after operation and using all recommended scales for the international survey of DBS.

Results: The degree of forward flexion of the spine has substantially decreased and the quality of life, motor symptoms and functioning improved in both patients.

Conclusion: STN DBS should be considered as a potential treatment option for PD patients with camptocormia. Further analysis is needed to conclude what PD patients are candidates for bilateral STN or GPi stimulation in the treatment of camptocormia.

#8547

Morbidity and Comorbidity of Deep Brain Stimulation – A Fourteen-Years Retrospective Cohort Study

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Keywords: Morbidity, Comorbidity, Deep brain stimulation.

Objective: To assess the surgical morbidity and comorbidity in patients with various disease entities of movement disorders,

epilepsy and obsessive-compulsive disorders that underwent deep brain stimulation (DBS) in a single DBS center of Taiwan.

Methods: From Feb 2002 to May 2016, a total of 191 patients in our institute were included for analyzed retrospectively. All patients underwent standard DBS procedures with intra-operative microelectrode recordings.

Results: Among surgical morbidity, symptomatic hemorrhage 2.1% (4/191), lead mal-positioned 2.6%(5/191) and hardware infection 2.6% (3/191). There had no surgical related mortality. In STN-DBS for Parkinson's disease (N = 158), post-operative general surgical morbidity was 36.1% (57/158), which included: weight gain (more than 5 kg) 25.3% (40/158), mania/hypomania 7.6% (12/158), transient confusion 7.0% (11/158), depression 3.8% (N = 6) and pulmonary edema 1.9% (3/158). Stimulation related morbidity was 41.8% (N = 66), which included hypophonia 15.8% (N = 25), dyskinesia 12% (19/158), dysarthria 12% (19/158), sialorrhea 10.8% (17/158) and decreased memory 10.1% (16/158). The comorbidity within the follow-up period up to 14 years was 51.4% (72/140), which included patients who expired, demented, received bone/spine surgery and diagnosed as cancer. Eighteen patients were loss from follow-up.

Conclusions: The associated morbidity and comorbidity was significant in DBS patients. Stimulation related morbidity was high in PD STN-DBS, nevertheless, most of these was transient, and could be improved after change in stimulation parameters. Though the incidence of intracranial hemorrhage was low, it remained as a high risk morbidity in DBS surgery.

#8548

Effect of Provocation Test on Heart Rate and Mean Arterial Pressure during Subthalamic Deep Brain Stimulation with General Anesthesia

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Keywords: Subthamamic deep brain stimulation, General anesthesia, Median nerve stimulation, Heart rate, Mean arterial pressure.

Background: We have proved in our previous report that dorsolateral subthalamic (STN) neuronal activity enhanced by median nerve stimulation (MNS) could characterizes Parkinson's disease during deep brain stimulation with general anesthesia. However, the vigorous passive range of motion test (PROM) and/or intense MNS might exert awakening effects to the patient who was lightly anesthetized.

Purpose: To find the most effective way to identify the sensory-motor portion of STN, yet, with less stimulation effect to the depth of anesthesia during microelectrode recording (MER).

Method: Prospective study (TCRD 104-35, IRB 103-122-A, Tzu Chi General Hospital, Hualien, Taiwan) A 3T MR image was used for pre-op target planning. In which, will be fused to CT scan with frame-based localizer at the day of surgery. Regular induction and endotracheal intubation for general anesthesia was performed, and then maintained with volatile anesthetic agent and muscle relaxant only. The depth of anesthesia was monitored by heart rate (HR), mean arterial pressure (MAP), and minimal alveolar concentration (MAC) of the volatile anesthetic agent. Neuronal firings were recorded within STN. Provocation test of PROM, MNS were performed at random.

Result: A total of 13 patients were enrolled in this study. Mean age at surgery and disease duration were: 55.6 ± 9.4 year-old and 8.8 ± 2.4 years, respectively. Average MER trajectory was 1.0 ± 0.2. Recorded depth of STN was 5.4 ± 0.7 mm. Depth of anesthesia was maintained within 0.5~0.9 MAC (0.7 ± 0.1 MAC). A total of 1113 neuronal firings were recorded (N = 642 without test; N = 106 with PROM; N = 236 with MNS; N = 129 with both PROM+MNS). When compared to baseline (without test), PROM significantly increased HR by 2.7344 (p = 0.0043), MAP by 2.4400 (p = 0.0175). MNS significantly increased HR by 2.0878 (p = 0.0028) and MAP by 7.8896 (p = 0.0000). When PROM and MNS were performed consecutively, HR significantly increased by 6.2645 (p = 0.0000), and MAP by 7.3521 (p = 0.0000). However, no patient was apparently awakened during the provocation test of MER procedures.

Conclusion: During MER for STN-DBS, median nerve stimulation could be an effective, yet convenient and save provocation test to identify the sensory-motor topography of STN. Though MAP was significantly higher than PROM during MNS, it was brief and transient. No apparent wakefulness was noted in all patients.

#8550

Bilateral Gpi-DBS in Belly Dancer's Dyskinesia

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Keywords: Deep brain stimulation, Dyskinesia, Dystonia, Motion analysis, Globus pallidus.

Belly dancer's dyskinesia (BDD) is a kind of focal dyskinesia affecting the abdominal wall and also may include diaphragmatic myoclonic jerks (or flutter) which can result in chest and/or abdominal pain and dyspnoea. Clinically, frequent, intermittent and often rhythmic involuntary undulations of the abdomen are observed. Several pathological conditions described in the literature, including idiopathic and psychogenic cases.

A 36-year-old woman presented with a 7-year history of daytime involuntary abdominal dyskinetic movements. The repeated local Botulinium toxin injections had minimal temporary beneficial effect. Cranial and spinal MRI failed to show circumscribed lesion, all laboratory tests including copper, ceruloplasmin, thyroid, and blood smear were unremarkable.

Fluoroscopy confirmed diaphragmatic contractions on both sides. The clinical symptoms were evaluated according to the Burke-Fahn-Marsden (BFM) dystonia rating scale. The dyskinesia

were recorded prior and after surgery and measured with infrared video-based computerized real time passive marker-based analyser of motions (RTPAM) with the sampling rate of 50/s. One midline and 8-8 lightweight retroflective markers were placed on both sides as abdominal landmarks. The detailed motion analysis with spectrograms has been performed with a software implemented in MATLAB (Mathworks, Sherborn, MA, USA).

As drug approaches were only of transient and limited effect, the patient was selected for surgery Bilaterally quadripolar leads (model 6147, St. Jude Medical, Inc., USA) were implanted to the posteroventral lateral GPi with a frameles MRI to frame-based CT fusion guided (Vister 3D home-developed planning software) stereotactic method (MHT system, Bad Krozingen, Germany). Intraoperatively bilateral microrecording (Neurospot, Neurostar, Tübingen, Germany) and stimulation screening has been used for refinement of optimal electrode tip position. In the same session under general anaesthesia the electrodes were connected to Brio dual channel rechargeable neurostimulator, implanted bilaterally in the subclavicular region. In the postoperative period no surgery-related side effects were observed. Postopertaive high resolution CT-scanning confirmed the proper electrode position.

The BFM score showed a total reduction of abdominal dyskinesia at 6-months, and long lasting benefit at the 1-year follow-up. RTPAM showed substantial regression of acceleration for all markers, and abolishment of the dominant frequency of the dyskinetic movements. The cross-coherence and correlation between symmetrical markers, and between markers within the right and left sides, significantly was decreased.

Conclusions: Bilateral GPi-DBS can be considered as a treatment option in belly dancer's dyskinesia. RTPAM is a useful tool for registration of involuntary abdominal movements and for detection of treatment effectiveness.

#8551

Porting a Smartphone Tremor App to Smartwatch for Telemonitoring

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Keywords: Tremor, DBS, Smartphone, Smartwatch, Telemonitoring, eHealth.

TREMOR12 is a smartphone app developed for measuring tremor. It measures 4 parameters (acceleration, rotation, rotation speed, and gravity) in 3 axes (X, Y, Z). All samples are time-stamped and measurements are performed at approximately 100 Hz. In contrast to other available smartphone apps that serve this purpose, TREMOR12 allows to export the raw data as comma-separated value (CSV) file for offline analysis. The purpose of this app is to expand tremor quantification beyond the level of frequency and amplitude by searching for detailed patterns that correlate to diagnostic or therapeutic consequences.

The obvious drawback of a smartphone application for tremor measurement is the practical limitation to perform chronic measurements during daily life activities. A smartwatch-based app would be more portable and suitable for chronic measurements. However, specific concerns arise when porting a smartphone app for tremor measurement to a smartwatch app meant for telemonitoring of tremor. Concerns relate to battery drainage, data transfer, device capacities and sampling strategies.

We will present our preliminary experience with these issues when porting TREMOR12 to a smartwatch-based app for chronic telemonitoring of tremor.

#8552

A Comparison Between Deep Brain Stimulation for Essential Tremor in the Ventral Intermediate Nucleus vs. the Posterior Subthalamic Area

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Keywords: Essential tremor, Ventral intermediate nucleus, Posterior subthalamic area.

Background: The ventral intermediate nucleus (Vim) of the thalamus is the traditional target for Deep Brain Stimulation (DBS) for the treatment of pharmacologically refractory essential tremor (ET). Recent evidence suggests that the posterior subthalamic area (PSA) might be a better target for tremor reduction. The PSA contains the dentato-rubro thalamic tract (DRTT), also called the cerebellothalamic tract, which is the main fiber bundle that forms the superior cerebellar peduncle. Previous studies demonstrated a significant correlation between the degree of connectivity to the DRTT at the stimulating electrode and the reduction of tremor.

Objective: To compare the effect of the Vim and the PSA as a target in a consecutive series of patients with a DBS treatment for ET. The efficacy outcome will be investigated by means of clinical parameters.

Methods: Twenty patients with a clinical diagnosis of ET were included in this retrospective study. All patients underwent bilateral DBS, in 15 patients Vim was used as DBS target, while in 4 subjects PSA was used. In one subject the Vim was targeted on one side, and the PSA on the other side. The outcome was measured by using the Essential Tremor Rating Scale (ETRS) and the Glass scale. At the same time quality of life assessment took place, using the Quality of Life in Essential Tremor questionnaire (QUEST) score. The coordinates of the active contacts were determined by analysing the post-operative imaging using the iPlan Stereotaxy software (Brainlab AG, Germany).

Results: Currently we are analysing the data and we will have the final results by mid July. We will present results regarding the outcome differences expressed in ETRS, QUEST and Glass scale in relation to the selected target. In addition, reported side-effects will be compared. Our preliminary results suggest that stimulation

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in the Vim target has better outcome regarding the ETRS reduction (%) and QUEST score in comparison to the PSA stimulation. Regarding the Glass scale, no significant difference has been discovered.

Conclusion: Based on our preliminary results both the ventral intermediate nucleus and the posterior subthalamic area are effective in reducing tremor. Whether one target is superior to the other is currently being investigated. These results will be presented during the meeting.

#8560

Long-Term Follow-Up of Combined Thalamic and Pallidal Stimulation in a Dystonic Head Tremor Patient Using a Novel Deep Brain Stimulation Device

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Keywords: Dystonia, Tremor, Deep brain stimulation, Multifocal DBS, Thalamus, Globus pallidus, Current steering.

Selected patients undergoing deep brain stimulation (DBS) may benefit from simultaneous stimulation of different anatomical targets. In the past the capabilities of available DBS devices were limited to two leads with total 8 contacts, and optimal programming employing multiple stimulation frequencies had required the implantation of two separate pulse generators. Thus, in September 2011, we chose to implant a novel, rechargeable DBS device (Synapse™ System, Nuviant Medical, Niel, Belgium), in a 35 year-old male suffering from medically refractory dystonic tremor associated with torticollis and irregular myoclonic jerks of the head and both arms. The system is based on 16 independent current sources for stimulation, and supports the placement of four 4-channel leads enabling differential control of 4 leads (diameter, 1.3 mm; electrode height, 1.25 mm; distance, 0.5 mm) that were placed bilaterally into the ventrolateral thalamus (VIM) and bilaterally into the globus pallidus internus (GPi) in a single session under local anaesthesia. Stimulation was kept off until a microlesioning effect had resolved after four weeks. Bilateral monopolar VIM stimulation was initiated (2.4 mA, 90 microsec, 180 Hz) at four weeks post-implant, and resulted in an immediate near-complete resolution of tremulous and irregular-jerky head motions that has been maintained up to the last followup in June 2016. At approximately 17 weeks post-implant, bilateral monopolar GPi stimulation was added for the relief of the remaining cervical dystonia and intermittent myoclonic jerks. GPi stimulation was continued bilaterally with 1.6 mA (left GPi) and 1.8 mA (right), 90 microsec and 130 Hz to date. Symptom relief has been sustained for almost 5 years until the last follow-up in June 2016, and it is dependent on stimulating both targets. Tremor recurred immediately after cessation of VIM thalamic stimulation. This new device represents a technological advance in the field of neurostimulation and has proven to be reliable and effective for the long-term application of multifocal DBS. As DBS targets may require specific stimulation parameters devices such as Synapse™ will be useful for the conversion of 'competing' DBS targets into 'complementing' targets.

#8562

Clinical Improvement in Deep Brain Stimulation with the Use of the O-Arm

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Keywords: iCT, DBS, UPDRS-III, MER.

The O-arm surgical imaging system® is a multidimensional platform that provides the opportunity of visualizing the electrodes in real time in deep brain stimulation surgery. The objective of this study is to investigate in our center the value of this tool, by comparing the clinical improvement of a group operated on with this technology and a control group. After one year follow-up, the results were analyzed.

Material and Methods: Twenty consecutive Parkinson disease patients that received deep brain stimulation with one year follow-up were selected. Electrode placement was optimized using the O-arm imaging system. They were compared to 20 consecutive patients operated on under 2D fluoroscopy as a control group. In both groups variation of the motor part of the Unified Parkinson's Disease Rating Scale (UPDRS-III) was measured, in addition to the number of microrecording tracks and the length of the surgery.

Results: A median basal off reduction of 42% was observed in the O-arm group vs. 24% in the control at one year follow-up, which was statistically significant ($p < 0.005$). The reduction of the length of the surgery was statistically significant, being 1 h and 10 minutes less in the O-arm group. The number of tracks needed per electrode was reduced from 2.47 to 1.99.

Conclusions: The O-arm can be easily included in the workflow of deep brain stimulation surgery. It gives the opportunity of visualizing the electrodes in real time. In our center it has helped to improve our results and refine our procedure. It has helped reducing the surgical time and number of tracks, as well as improving the clinical state of our patients. Further studies are needed to establish the fusion error.

#8563

Objective Quantification of Rigidity during Deep Brain Stimulation Surgery

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Keywords: Rigidity, Deep brain stimulation, Objective quantification.

The evaluation of both therapeutic- and adverse effects of test stimulation is normally regarded as the most important factor during deep brain stimulation surgery when deciding whether or not the electrode placement is satisfactory. Symptom evaluation is usually performed by a neurologist, who relies on experience and knowledge to provide a subjective measure of the evaluated parameters. However, several studies have shown that clinical evaluations of symptomatology of movement disorders is accompanied by both inter- and intra-rater variability (Little 2012, Kwon 2014). Objective quantification of baseline symptomatology as well as changes in symptoms due to electrode placement and subsequent stimulation can contribute to reduce this variability and further improve surgical accuracy and more importantly clinical outcomes. The aim of our study is to investigate the practicality and sensitivity of a tailor made wrist rigidity device for the objective assessment of resistance to passive wrist movement during DBS surgery.

Our device consists of an acrylic mechanical system with a potentiometer built into the low friction hinge between a hand- and forearm-plate that measures wrist joint angle. The hand is positioned between two acrylic cylinders and forearm is secured to a separate plate using straps, allowing only a flexion/extension movement in the wrist joint. The hand-plate also includes a handle with an integrated bi-directional force-gauge for the examiner to perform the wrist flexion/extension movements by moving the hand-plate. Appropriate measurements are taken at three time points during surgery with and without contralateral co-activation (simultaneously squeezing the other hand) 1) before insertion of the electrode 2) directly following insertion prior to test stimulation and 3) during test stimulation at target level. Our measures do not replace the standard clinical evaluations by the neurologist, but instead are performed complimentary to standard assessment. Each measurement consists of 12 flexion/extension movements by the examiner at a constant pace of 50 beats per minute, dictated by a metronome.

We have currently collected rigidity data from 2 volunteers. The first dataset was recorded from a patient with Parkinson's disease who had already undergone DBS 6 months earlier. We assessed the rigidity of this patient in a medical ON and OFF state followig a routine clinical consultation. The second patient was recorded during surgery at the three time points described earlier. We intend to collect data for this pilot study from at least 5 more patients using the device and aim to present a detailed report of the results at the time of the XXII Congress of the European Society for Stereotactic and Functional Neurosurgery in October this year.

If proven practical and effective, these methods could supplement and improve the current subjective assessments during surgery and set a new standard, but also contribute to predict clinical outcomes and improve patient management.

#8567

Deep Brain Stimulation Site Relative to the MER-Defined STN One Year after Surgery Predicts Motor Improvement in PD

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Keywords: Deep brain stimulation, Subthalamic nucleus, Motor improvement.

Introduction: Deep brain stimulation (DBS) of the subthalamic nucleus (STN) is a widely used surgical treatment for severe Parkinson's disease (PD). However, post-operative motor improvement can vary greatly between patients, which might be caused by varying locations of the stimulating contact point. Research into the relation between motor improvement and active contact point (ACP) location using standard anatomical landmarks (AC-PC) may suffer from inaccuracy caused by anatomical variations between patients. Studies using the MRI-defined STN may also suffer from inaccuracy because the STN can be hard to identify in preoperative MRI. Therefore, in this study, we use the intraoperative microelectrode recordings (MER) to create a detailed estimation of STN size and location and then study the relation between motor improvement and ACP location relative to this MER-defined STN.

Methods: For this study, we used 43 STNs of 26 patients, from the Dutch NSTAPS trial that had 1) assessment of PD motor symptoms preoperative and one year postoperative, 2) CT imaging of the implanted lead one year postoperative and 3) intraoperative MER that measured STN activity on at least three channels.

STN size and location was estimated by automatically transforming a general biconvex lens-shaped STN to fit optimally on the MER measurement sites scored as either inside or outside the STN. The one year postoperative CT was fused with preoperative T1 MRI including stereotactic frame, stereotactic ACP location was manually determined and combined with the patient specific MER-defined STN. Finally, the STN and the ACP location together were transformed back to the original biconvex lens shape. This way, the ACP locations of the entire group could all be studied relative to one general STN shape.

Per STN, the DBS-induced motor improvement was defined as the combined off-levodopa improvement on the UPDRS III of strictly contralateral motor symptoms as a percentage of the preoperative combined contralateral off-levodopa UPDRS III score.

Location data was statistically analyzed using both standard multiple regression and independent samples T-tests. For the latter, two groups were defined based on the percentage of motor

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improvement: DBS-responders who showed a contralateral improvement of 50% or more (n = 27) and non-responders who improved less than 50% (n = 16).

Results: For the group of DBS-responders, the mean ACP location one year after surgery was 0.8 mm lateral, 1.5 mm anterior and 2.1 mm dorsal to the center of the MER-defined STN. Independent samples T-tests showed that the ACP location relative to the general STN in the non-responder group was significantly more medial (smaller x-coordinate) than in the responder group ($p = 0.045$). No significant differences were found in the y- and z-coordinates representing the anterior-posterior and the dorsal-ventral directions respectively.

Standard multiple regression showed that the x-, y- and z-coordinates of the ACP location together explain 37% of the variance in contralateral motor improvement (adjusted R square = 0.365, $p < 0.0005$). Further evaluation of the three directions in this regression showed that both the x- and the z-coordinates of ACP location made a significant unique contribution to the prediction of motor improvement. A more medial ACP location had the most pronounced negative contribution to the prediction of motor improvement (beta = –0.66, $p < 0.0005$), thus predicting less motor improvement. A more dorsal ACP location also predicted less motor improvement although its contribution was smaller (beta = –0.36, $p = 0.016$).

Discussion: In this study we showed that a relation between ACP location and motor improvement can be found when determining the ACP locations relative to the MER-defined STN. The advantage of this method is that it takes into account the anatomical variations in STN location without depending on high quality MRI images.

In DBS surgery it is important to target the anterior part of the dorsolateral STN, which corresponds to the sensorimotor area. Stimulation on contacts that are located more medial or more dorsal results in significantly less motor improvement. This has implications for both the lead placement during surgery and the postoperative selection of contacts for stimulation. During surgery, the MER-defined STN could be helpful in preventing too medial implantation and during contact selection the MER-defined STN could be used to prevent too dorsal stimulation.

#8569

Functional Brain Imaging of DBS-Treated Essential Tremor

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Keywords: Essential tremor, Deep brain stimulation, fMRI.

Background: Essential tremor (ET), characterised by postural and/or action tremor, is the most common movement disorder. The pathophysiology of ET is poorly understood. However, several brain regions along the cerebello-thalamo-cortical network have been hypothesised to be involved in the generation of tremor oscillations. Evidence for involvement of different regions within this loop has been derived from various animal, neuropathological, structural and functional neuroimaging studies.

ET can be disabling to the grade of necessitating invasive Deep Brain Stimulation (DBS). DBS in the caudal zona incerta (cZi) has shown a considerable reduction in tremor for patients with otherwise medically intractable tremor. The mechanisms underlying the effects of DBS remain unclear.

Objectives: Investigating, by using blood oxygenation level-dependent functional magnetic resonance imaging (BOLD fMRI), whether regions within the cerebello-thalamo-cortical network are influenced by therapeutic DBS during tremor-inducing movements.

Methods: Fourteen patients with cZi-DBS for ET underwent 1.5T fMRI. During fMRI, the patients executed right arm tremor-inducing movements (postural holding and aiming movements) as well as a baseline resting task. Tremor and hand movements were recorded by an MR-compatible single-axis accelerometer attached to the ulnar side of the right hand.

The tasks were performed with the stimulation turned on and off, with the initial stimulation setting (on/off) counterbalanced across patients. The fMRI design consisted of three blocks (postural, aim and rest) with 20 seconds duration and 10 repetitions each. fMRI data were pre-processed and analysed using a general linear model implemented in SPM12.

Results: Clear therapeutic effects of cZi-DBS, in terms of tremor intensity reduction, were measured by the accelerometer in patients with ET. Preliminary fMRI analysis showed interaction effects between postural holding and DBS where BOLD activity increased in the posterior parts of the middle and inferior frontal gyrus when performing postural holding while DBS was turned on.

Interaction effects between postural holding and DBS, mainly driven by DBS effects during the resting condition, were also seen as increased BOLD activity in primary motor cortex, premotor cortex and cerebellum when performing postural holding while DBS was turned on. On the other hand, BOLD activity decreased in Crus I within the ipsilateral cerebellum when performing the same task while DBS was turned on. The latter effect within the cerebellum was mostly driven by DBS actions during the postural holding.

The average effect of DBS across all conditions (postural, aim and rest) was observed as an increased BOLD activity in frontotemporal areas bilaterally, mostly outside the motor network.

Conclusions: Effects of therapeutic cZi-DBS observed as modulated BOLD activity in several frontotemporal regions including the motor network and also in the cerebellum. This study supports the notion of DBS acting upon modulation of the cerebello-thalamo-cortical loop in ET.

#8574

The Effect of Bilateral Subthalamic Deep Brain Stimulation on Cognitive Functions in Parkinson's Disease

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Keywords: Parkinson's disease, DBS, Subthalamioc nucleus, Cognitive functions, Frontostriatal networks.

Objective: The present study was conducted to assess the effect of bilateral subthalamic nucleus (STN) deep brain stimulation (DBS) on cognitive functions in PD patients using a PD control group.

Methods: All PD patients included in study fulfilled the UK Parkinson's Disease Society Brain Bank clinical diagnostic criteria for PD. Ten wait-listed patients PD patients (control group) and 10 PD patients with DBS implantation (DBS group) participated in the study. Surgical procedure was based on planning with custom-developed Vister-3D software frameless MRI to CT image fusion and with RM and MHT stereotactic systems. Intraoperatively 3 to 5-channel microelectrode recording has been applied with registration of Neurospot (Neurostar) recording equipment. Model 3389 electrodes were implanted bilaterally in all cases and were connected to Activa PC dual channel implantable pulse generators.

A neuropsychological battery was used to assess cognitive functions, including general mental ability (Mini Mental State Examination), verbal (digit span) and spatial short-term memory (Corsi block-tapping task), working memory (n-back task) and executive functions (phonemic and semantic verbal fluency, Stroop task, Trail Making B task). Each task was administered twice: before and after surgery in the DBS group with the stimulators on and with a similar time interval between the two task-administration points in the control group.

Results: There was no significant difference between the DBS and the control groups' performance in tasks measuring the main cognitive functions. The DBS group showed a significant decline only on the semantic verbal fluency task after surgery compared to its own baseline level ($p < 0.05$).

Conclusions: Our results are in line with findings of previous studies. The findings are discussed considering different possible effects of the STN DBS on frontosriatal networks.

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#8575

Retrospective Evaluation of the Non-Linear Whole-Brain MNI152 Atlas Registration for Vim-DBS Targeting

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Keywords: Thalamus, Deep brain stimulation, Non-linear registration, Brain atlas.

Background: Despite of the expressive development of the diagnostic imaging in the last decades, the stereotactic targets of the thalamus are still considered invisible. At present stereotactic atlases still used based on indirect methods for planning ventrointermediate (Vim) nucleus – deep brain stimulation (DBS) surgery.

Objectives: Retrospective study to evaluate the ability of non-linearwhole-brain MNI152 atlas registration to improve individual targeting, of the 'tailor-made' anatomical fusion suitable for preoperative planning.

Methods: 15 patients – altogether 25 implanted DBS leads – with pure essential tremor were treated with Vim-DBS. The tremor score was assessed pre-and postoperatively. The tremor amplitude reduction reached 90% in the follow-up period. The position of the active contacts were allocated in the postoperative CT-space and thereafter the non-linear registration in the MNI152 standard space with FMRIB Software Library. The registrations were verified manually with visual control. All of the active contact's position were measured in three planes in the registered MNI152 standard space and patient individual CT-space. References were the intercommissural line, the third ventricle wall, the AC-PC plane and we calculated (target-PC)/(AC-PC) ratio.

Results: In our investigation the standard deviation of the active contact position in the MNI152 atlas space was reduced in each plane compared with the patient's individual space. In addition, we found numerous locations of the active contacts wide of the ideal anatomical lead trajectory in the MNI152 standard space, after successful registration. In this case the 7 mm or wider third ventricle in AC-PC, the unparallel or irregular third ventricle wall was considered. The AC-PC distance, the cerebral atrophy, the shape of the cranium had no effect on the fine registration of the thalamus.

Conclusions: The non-linear whole brain atlas registration before the operation would provide useful tool for stereotactic atlases based 'individual' planning for Vim-DBS surgery in selected population.

Acknowledgement: This work was supported by research grant KTIA_NAP B_13-2-2014-0020.

#8579

Comparison of Battery Longevity in Two Commonly Used Implantable Pulse Generators for Deep Brain Stimulation

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Keywords: Deep brain stimulator, Implantable pulse generator, Battery longevity.

Objectives: Deep brain stimulators consist of a quadripolar electrode implanted in the brain parenchyma connected to an implantable pulse generator (IPG). The IPG acts as both power source and waveform generator. Non-rechargeable IPG's require periodic replacement at the end of battery life, which carries both surgical risks and financial implications. Advancements in battery technology have led to replacement of the widely used Medtronic Kinetra with the Activa PC IPG system. Although previous studies have compared battery life in single channel DBS systems and in the treatment of different neurological conditions there has been no analysis of dual channel DBS systems[1,2]. We have therefore compared battery life in these two commonly utilised dual channel IPG systems and whether choice of DBS target and pathology impacts on battery drainage. This may inform choice of DBS systems depending on the underlying disease process.

Methods: All patients who underwent insertion of DBS in our neurosurgical centre were identified from a centrally recorded database. Only those who had insertion of bilateral Medtronic Kinetra or Activa PC DBS stimulators for STN stimulation to treat Parkinson's disease (PD) or GPi stimulation to treat Dystonia were included in the final analysis. Time between replacement of IPG systems due to low battery life was recorded in days. Battery life was then assessed using a Kaplan-Meier approach, with those patients whose batteries had not been replaced by the end of follow-up censored at this point. The median (95% Confidence Interval) battery life was then estimated from the Kaplan-Meier curves, and comparisons between groups made using log-rank tests. Statistical analysis was performed using IBM SPSS 22, with $p < 0.05$ deemed to be statistically significant.

Results: Data was available for 183 patients with bilateral STN DBS stimulators for PD and 11 patients with bilateral GPi stimulators for dystonia. For the treatment of PD the Kinetra cohort ($N = 83$), had a median battery life of 6.6 years (95% CI: 6.5–6.7). This was significantly longer than the Activa PC cohort ($N = 100$), which had a median battery life of 4.5 years (95% CI: 4.4–4.5) ($p < 0.001$). Six patients in the Activa PC group had the interleaving programme applied for the treatment of PD, resulting in a significantly shorter battery life of 3.7 years (95% CI: 2.7–4.8).

Data were available for an additional 5 Kinetra patients with dystonia who had a battery replacement. A significant difference in battery life was detected between the groups ($p < 0.001$), with a median battery life of 3.7 years (95% CI: 2.3–5.1) in patients with dystonia, compared to 6.6 years (95% CI: 6.5–6.7) in those with PD.

Conclusions: The Activa PC IPG demonstrates a significantly reduced battery life of 2.1 years in comparison to the Kinetra IPG in STN stimulation for PD. Use of the interleaving function led to a further significant decrease in the Activa PC battery life by a median of 0.8 years. In addition, stimulation of GPi for treatment of dystonia results in a significantly shorter battery life of 2.9 years when compared to STN stimulation for PD in the Kinetra cohort, suggesting the DBS target and underlying pathology impacts on battery drainage. The clinician should therefore carefully consider potential battery life of the IPG system being used when treating different neurological conditions. Use of rechargeable DBS systems for management of dystonia may be more appropriate if the patient is able to comply with recharging, aiming to reduce the morbidity associated with more frequent IPG replacement.

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#8580

Management of Traumatic Subdural Hematoma in a DBS-STN Patient

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We describe an 61-year-old male with twelve year history of idiopathic Parkinson Disease who underwent for bilaterally STN. 3 days after surgery he was discharged without any complication. Two days later he was admitted to emergency department after a car accident. No abnormality was detected in his neurological examination except symptoms of parkinsonism. Cranial CT of patient revealed a hyperdense left acute subdural hematoma (SDH) with a midline shift of 8 mm. He was hospitalized and follwed-up clinically and radiologically. No increment was detected radiologically in the size of hematoma. Repeated CT scans demonstrated progressive resolution of the hematoma. When SDH was completely absorbed the DBS battery has been run. No side effect was observed and the optimal response of DBS was achieved. Our case showed that although there is a potential risk of electrode displacement due to SDH, urgent surgical evacaution must not be considered immediately.

There are no established guidelines for the management of subdural hematoma in patients with DBS implantation. With a subdural hematoma, the brain will shift ventromedially; since DBS leads

are tethered to the skull, the ipsilateral lead will have a relative dorsal displacement from its original target site (1). In the literature rewiew the authors stated that, ıf a life-threatening conditions develops due to SDH, surgical evacuation should be recommended as the fisrt option and check the electrodes radiologically and electrophyscology. İn our case, there was no neurological findings depends on subdural hematoma thus only neurological and radiological follow was sufficient.

#8593

Novel Insights into the Basal Ganglia: Visualisation of the Micro-Circuitry by Ultra-High Field MRI of the Post Mortem Human Brain

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Keywords: Subthalamic nucleus, Substantia nigra, Globus pallidus, Post mortem, Ultra-high field MRI, Tractography.

Introduction: The subthalamic nucleus, substantia nigra, and globus pallidus, three nuclei of the human basal ganglia, play an important role in motor, associative, and limbic processing. The network of the basal ganglia is generally characterized by a direct, indirect, and hyperdirect pathway. This study aims to investigate the mesoscopic nature of these connections between the subthalamic nucleus, substantia nigra, and globus pallidus and their surrounding structures.

Methods: A human post mortem brain specimen including the substantia nigra, subthalamic nucleus, and globus pallidus was scanned on a 7 T MRI scanner. High resolution diffusion weighted images were used to reconstruct the fibers intersecting the substantia nigra, subthalamic nucleus, and globus pallidus. The course and density of these tracks was analyzed.

Results: Most of the commonly established projections of the subthalamic nucleus, substantia nigra and globus pallidus were successfully reconstructed. However, some of the reconstructed fiber tracks such as the connections of the substantia nigra pars compacta to the other included nuclei and the connections with the anterior commissure have not been shown previously. In addition, the quantitative tractography approach showed a typical degree of connectivity previously not documented. An example is the relatively larger projections of the subthalamic nucleus to the substantia nigra pars reticulata when compared to the projections to the globus pallidus internus.

Discussion: This study shows that ultra-high field post mortem tractography allows for detailed 3D reconstruction of the projection of deep brain structures in humans. Although the results should be interpreted carefully, the newly identified connections contribute to our understanding of the basal ganglia.

#8598

Experience of Deep Brain Stimulation for Dystonia Treatment in Tyumen

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Keywords: Deep brain stimulation, Tyumen Russia Dystonia.

Dystonia is one of the most common disorders in clinical practice of movement disorders. Dystonia is typically considered a movement disorder characterized by motor manifestations, primarily sustained or intermittent muscle contractions causing abnormal, often repetitive, movements, postures, or both.

It can be very disabling, especially in young, socially active patients.

Medical treatment of multifocal, generalized and segmental dystonia is very difficult, because medications have very low effect. Botulinum toxin was considered as an effective treatment of focal and segmental forms of dystonia. Sometimes needed very hi-gh doses of botulinum toxin for clinical effect or patient develops resistance to it.

From 2012 in Federal center of Neurosurgery, Tyumen deep brain stimulation established as medical option for treatment of movement disorders, pain, epilepsy. Since 2012 to 2015 there was treated 58 patients with dystonia resistant to previous medical treatment.

Over 40 deep brain stimulation systems were implanted to treate dystonia patients and 18 generators replaced for previously operated people. Of 40 patients 36 operated because of primary dystonia (focal – 2, segmental – 5, multifocal – 7, generalized – 22), secondary dystonia – 4 patients (2 of them with tardive dystonia). In our study we used Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS), Cervical Dystonia Impact Scale (CDIP-58), Fahn-Marsden Dystonia Rating Scale (FMDRS). All patients were divided into four groups (depending on the clinical effect): excellent improvement – 35%, good– 32.5%, moderate– 27.5%, unsatisfactory– 5%. There was no surgical complications. The effect of stimulation was stable in all patients (4 patients with severe dystonia had recurrence of symptoms after switching off stimulation). We did not observe serious adverse events during stimulation.

In our series deep brain stimulation considered as safe and effective treatment of primary dystonia and secondary dystonia.

#8602

Subcutaneous Fibrosis Around Extension Cables in DBS – Case Report and the Literature Review

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Keywords: DBS, Fibrosis, Complications.

The authors present the case of patient with subcutaneous fibrosis, which developed around extension cables in patient treated with DBS for essential tremor, 5 months after surgery. The fibrosis limited the movement of the neck and during head rotations, it caused pain in the scalp, especially around the scars above Stimlocks. Painful sensations led to removal and replacement of extension cables along different subcutaneous trajectory. Overview of published literature is analysed with a proposal of the solution of abovementioned complication.

#8603

Intraoperative Quantitative Tremor Evaluation in Deep Brain Stimulation Surgery

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Keywords: Deep brain stimulation, Intraoperative monitoring, Acceleration, Tremor, Parkinson's disease, Essential tremor.

Background: Deep brain stimulation (DBS) is a common neurosurgical treatment for the tremor of Parkinson's disease, essential tremor, and tremor of other causes. The outcome depends on optimal placement of the permanently implanted electrode. Many centers perform DBS surgery under local anesthesia in order to confirm the therapeutic effect with intraoperative stimulation testing. Visual inspection—the method generally used to rate changes in tremor during stimulation testing – is subjective, and its accuracy depends on the evaluator's experience [1]. This study presents the results of quantitatively estimating improvement in tremor during intraoperative stimulation tests in 15 patients. In addition, its influence on identifying the final position of the permanently implanted electrode is described.

Method: We designed a 3D acceleration sensor system that is attached to the patient's forearm during surgery [2]. During intraoperative stimulation tests, at each different position, accelerometric data are synchronously recorded with the changing stimulation current amplitude. The method was applied in 15 DBS procedures in 2 centers (University Hospital Bern, Switzerland & University Hospital Clermont-Ferrand, France); the data were analyzed offline to assess improvements in tremor and to identify tremor-suppressing stimulation current-amplitudes. For correlation analysis, the quantitatively and visually determined improvements in tremor were categorized into: no improvement, low improvement, average improvement, high improvement and tremor arrest. The quantitatively identified tremor-suppressing current-amplitudes were compared to those identified by visual inspection, in order to determine the influence these findings would have had on the position chosen for permanent electrode implantation if they had been used for intraoperative decision-making. As this was a purely observational study, the accelerometric measurements were not, in fact, allowed to alter the surgical procedures in any way.

Results: A total of 359 evaluations were available for a comparison of the improvement in tremor identified by accelerometry vs. visual inspection. Of these evaluations, 156 (43.5%) were assigned the same categorie by both methods; 296 (82.5%) fell in the same or neighboring categories; and 63 (17.5%) were at least 2 categories apart. The quantitatively identified tremor-suppressing current-amplitudes were significantly lower than the visually identified ones (1.13 ± 0.8 mA vs. 1.7 ± 0.8 mA [mean ± SD]). Of the 26 finally chosen positions for permanent lead implantation, 15 would have been different had the accelerometric data been considered.

Discussion and Conclusion: The improvement of tremor brought about by test stimulation was rated in the same category by visual inspection and by quantitative measurement (accelerometry) in only 43.5% of the evaluations that we made in this study. In some of the evaluations where there was only mild tremor at baseline, the stimulation-induced improvement in tremor was classified by visual inspection as tremor arrest, while accelerometry revealed a very mild residual tremor. This fact explains many of the instances in which the tremor ratings obtained by the two methods were only 1 category apart, but it cannot account for the 17.5% of evaluations that were 2 or more categories apart.

The quantitative assessment of tremor as performed here yields different findings from assessment by visual inspection alone. The tremor-suppressing stimulation current-amplitudes are lower, and this, in turn, can often affect the chosen site for permanent electrode implantation. Thus, quantitative tremor assessment can affect, and perhaps improve, targeting in DBS without altering the routine surgical procedure. This tentative conclusion awaits confirmation by further studies. Moreover, aside from its potential direct clinical utility, quantitative tremor assessment DBS surgery might be a useful adjunct to the clinical testing of new types of DBS electrode.

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#8605

Improving DBS Targeting Using 3D Visualization of Intraoperative Stimulation Tests

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Keywords: Deep brain stimulation, Essential tremor, Electric field simulations, Accelerometer, Visualization.

Background: In the past three decades, over 100,000 movement disorder patients like Parkinson's disease (PD) have been treated by deep brain stimulation (DBS). Despite an increasing use of DBS, the fundamental mechanisms underlying therapeutic and adverse effects as well as the optimal stimulation site remain largely unknown. Among other techniques, computational simulations of the distribution of electric entities have been used to analyze long term chronic stimulation results in relation to the anatomy surrounding the stimulating contact. To our knowledge such methods have never been applied to study clinical results obtained during intraoperative stimulation tests. Therapeutic effects of stimulation are in general visually evaluated based on subjective clinical rating scales which are known for their inter- and intra-rater variability. While very few research groups have attempted intraoperative quantitative tremor evaluation, no research group has used computational simulations of the distribution of electrical entities during such stimulation tests. This study presents a method to correlate simulations of the electric field distribution during intraoperative stimulation tests with quantitatively evaluated symptom improvement and patient specific anatomy to get more information regarding mechanisms of action and in turn optimize DBS target selection.

Method: During DBS surgery of 3 essential tremor patient at the University Hospital in Clermont-Ferrand, France, a previously developed accelerometer based quantitative tremor evaluation technique was used [1]. The ventro-intermediate nucleus (VIM) and its anatomic neighbors were manually outlined based on spontaneous MRI contrasts and using a high field (4.7 Tesla) atlas. For each paitient, two parallel trajectories were planned per hemisphere with 7–8 stimulation test positions per trajectory spanning the region of interest. During the intraoperative stimulation tests, accelerometer data were recorded in sync with the stimulation current amplitude. Tremor improvement was postoperatively quantified compared to baseline tremor. For two stimulation amplitudes (low and high improvement) per position the effect of intraoperative stimulation tests in relation to the patient's anatomy was studied along with the Department of Biomedical Engineering at Linkoping University. A computational model of the intraoperatively used exploration electrode was developed to simulate electric-field isosurface (0.2 V/mm) in the brain for the previously identified stimulation current amplitudes at the different test positions. Due to the large number of simulations, each voxel in the region of interest may be part of several isosurfaces-each surface depicting one amplitude responsible for one improvement in tremor. To simplify visualization and interpretation, a maximum improvement map was generated, where each voxel was assigned to the isosurface representing the maximum improvement. Anatomical images, delineated structures, trajectories and improvement maps were visualized together in Paraview (Vtk based visualization software). The resulting visualization was evaluated by clinicians.

Results: The software allowed 3D visualization as well as orthographic slices parallel to the trajectory. Clinicians confirmed that it enables the identification of the most effective stimulation areas with respect to the anatomy. A visual analysis of the improvement map for all the patients indicate that the highest improvement in tremor is observed when the region inferior, posterior and medial to the VIM is stimulated, i.e. the region where prelemniscal radiations merge with the VIM.

Discussion and Conclusion: The proposed concept based on quantitative tremor evaluation, electric field simulations and patient specific anatomical data proposed provides a unique way to visualize a multitude of information in an interactive and adaptable way. The application of the method to 3 patients shows that the region where prelemniscal radiations merge with the VIM may be optimal for reducing tremor. This is also observed by other researchers. By applying this new method on more patients, the analysis of a high amount of intraoperative data might help to elucidate the mechanism of action of DBS.

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#8606

Long-Term Follow-Up of Unilateral DBS of the Caudal Zona Incerta for Parkinsonian Tremor

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Keywords: Deep brain stimulation, DBS, Zona incerta, Tremor, Parkinson, Parkinson's disease.

Aim: The aim of this study was to evaluate the long-term efficacy of unilateral deep brain stimulation (DBS) of the caudal Zona incerta (cZi) for treatment of tremor-dominant Parkinson's disease (PD).

Method: 13 patients with medically refractory and predominantly unilateral tremor-dominant PD were included and assessed before surgery and at 1 year and at long term follow up 3–8 years after surgery. The mean age at the time of surgery was 67 years (range 59–75 years). The cZi was identified anatomically on stereotactic T2-weighted transaxial MRI images medial and slightly posterior to the visualized posterior tail of the subthalamic nucleus at the horizontal level of the maximal diameter of the red nucleus. The electrode location was verified with an intra-operative stereotactic CT. The patients were evaluated using the motor part of the Unified Parkinson Disease Rating Scale (UPDRS-III) combining OFF/ON medication and OFF/ON stimulation. Friedman's test was used for statistical evaluation of non-parametric values and the Wilcoxon signed rank test as a post-hoc analysis. Analysis of variance for repeated measurements was used for continuous variables with the Bonferroni correction method as a post hoc test. A p-value ≤ 0.05 was considered statistically significant.

Results: Long-term follow-up were performed at a mean time of 62 months after surgery.

Contralateral tremor-scores were reduced from 7.8 off med/off stim to 1.5 (80% $p \leq 0.001$) off med/on stim at one year and from 7.4 to 1.8 (76% $p \leq 0.001$) at long-term follow-up. The corresponding figures when combining stimulation and medication were 0.7 (91% $p \leq 0.001$) at one year and 0.9 (88% $p \leq 0.001$) at long-term follow-up.

Contralateral hand tremor at rest were reduced from 3.2 off/off to 0.5 off/on (86% $p \leq 0.002$) at one year and from 2.8 to 0.5 (82% $p \leq 0.002$) at long-term follow-up. The corresponding figures when comparing on med/on stim were 0.3 (90% $p \leq 0.002$) at one year and 0.1 (97% $p \leq 0.001$) at long-term follow-up.

Contralateral action-tremor were reduced from 3.4 off/off to 0.5 off/on (84% $p \leq 0.001$) at one year and from 2.9 to 0.8 (72% $p \leq 0.002$) at long-term follow-up. The corresponding figures when comparing on/on were 0.4 (89% $p \leq 0.001$) at one year and 0.6 (79% $p \leq 0.002$) at long-term follow-up.

Contralateral bradykinesia had a minor but significant reduction at both one year and long-term follow-up with stimulation alone. The symptom reduction was further increased when combining stimulation with medication.

Contralateral rigidity had a minor reduction at one year but the effect was non-significant at long-term follow-up both with stimulation alone and combination with medication.

Total UPDRS-III score was reduced from 42.5 off med/off stim to 27.7 off med/on stim (35% $p \leq 0.001$) at one year and from 46.5 to 35.4 (24% $p \leq 0.001$) at long-term follow-up. The corresponding figures on med/on stim were 17.2 (59% $p \leq 0.05$) at one year and 28.7 (38% $p \leq 0.002$) at long-term follow-up.

Mean stimulation parameters were 2.8 V, 71.5 uS and 148.5 Hz at one year and 2.7 V, 76 uS and 146.9 Hz at long-term follow-up. These differences were non-significant.

Conclusion: Unilateral cZi DBS continues to be an effective treatment for patients with severe Parkinsonian tremor even many years after surgery. The effect is pronounced regarding tremor, even if minor improvements are also seen regarding bradykinesia.

#8614

Differential Approach to Neurosurgical Treatment of Dystonia Patients

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Keywords: Primary (isolated), Neurodegenerative and acquired dystonia, Deep brain stimulation, Thalamotomy, Selective rhizotomy, Selective peripheral denervation.

Background: Dystonia is a heterogeneous group of movement disorders, which is specified by sustained or intermittent muscular contractions, causing involuntary abnormal movements and/or postures. Indications for neurosurgical treatment in dystonia include inefficacy/insufficiency of pharmacological treatment, widespread distribution of pathological movements, limitation in activities of daily living and self-service due to dystonic movements. Main clinical goal of the surgery is prevention of permanent disability and improving in the quality of life of dystonia patients.

Objective: To analyze the experience of neurosurgical treatment of dystonia patients in Burdenko Neurosurgical Institute.

Patients and Methods: 179 patients with different types of dystonia were operated in the period from 2003 to 2015: 56 patients with isolated (primary) generalized dystonia; 44 with isolated segmental dystonia; 41 with isolated focal/cervical dystonia; 7 with myoclonic or tremulous dystonia; 2 with basal ganglia calcification; 6 with the other neurodegenerative dystonia; 4 with tardive dystonia, 14 with dyskinetic cerebral palsy (CP); 5 with the other acquired dystonia. Disease duration ranged from 2 to 57 years; age at surgery ranged from 7 to 67 years. We assessed clinical outcome in patients with the minimum three-year follow-up available. Burke-Fahn-Marsden rating scale was used to evaluate dystonia severity. For cervical dystonia, TWSTRS and Tsui scales were applied. Postoperative changes in functional and motor state were assessed using Global outcome scale (GOS).

Results: Majority of the patients with primary (isolated) dystonia received DBS GPi (134 patients, 95%). Ten of them had a

history of previous stereotactic lesioning surgery. Main clinical improvement was observed in the first 6 months of DBS GPi. 86 patients were available for evaluation in long-term follow-up. Motor improvement in patients with generalized dystonia after 3 years was 59.7 ± 15.7%, in patients with segmental dystonia – 66.5 ± 17.5%, according to BFMDRS. In cervical dystonia, motor improvement after 3 years of DBS GPi was 55.5 ± 22.1%, according to TWSTRS, and 60.9 ± 19.9%, according to Tsui scale. 88% of patients had stable excellent or good motor and functional outcome in long-term follow-up (up to 12 years, GOS). Negative predictive factors for DBS GPi efficacy in primary dystonia appeared to be longer disease duration, earlier age of onset, and severity of motor impairment. Four patients required implantation of the second pair of GPi-electrodes for optimizing clinical outcome.

One patient with previous thalamotomy underwent bilateral DBS STN with 66% improvement.

In 6 patients with predominantly tonic pharmacoresistant cervical dystonia, selective peripheral denervation of cervical muscles was performed alone (3 patients) or in addition to DBS GPi (3 patients).

Among non-primary dystonia, high DBS GPi efficacy was observed in patients with tardive dystonia. Mean improvement in motor BFMDRS was up to 90%. In BGC-associated dystonia, initial response to DBS GPi was good, however, deteriorated in the later time course.

In the other neurodegenerative and acquired dystonia associated with structural brain lesions, functional outcome of DBS GPi was poor with minimal motor improvement.

In patients with predominant dystonic tremor or myoclonus and distal limb dystonia, DBS of ventral lateral thalamic nuclei was preferred.

Two patients with unilateral limb dystonia (incl. hemidystonia, action-specific/occupational dystonia) underwent unilateral Vop-thalamotomy with good functional outcome.

For dyskinetic CP patients, intrathecal baclofen pump therapy or selective combined (dorsal and ventral) rhizotomy was applied alone or in combination with stereotactic procedures (DBS or lesioning) and peripheral neurotomy.

Conclusion: At present, DBS GPi has the largest evidence of efficacy and safety for dystonia. Selection of the other surgical approaches and targets is possible on the individual basis. Thalamic targets are to consider in tremulous/myoclonic dystonia or limb dystonia. There is still no clear evidence for DBS of subthalamic nucleus in dystonia. Stereotactic lesioning procedures have limited application and need to be performed unilaterally to avoid neurological complications. Surgical outcome in non-primary dystonia varies individually; in CP, often staged surgical procedures are needed. For maximal efficacy the timeliness of surgical intervention is important. Preoperative evaluation of surgical candidates should be carried on by experienced multidisciplinary team.

#8617

Neurosurgical Management of Holmes-Tremor: A Multitarget Approach Using Advanced Planning Techniques

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Keywords: DTI, Holmes-tremor, Tremor, Tractography, DBS, Deep brain stimulation.

Introduction: Deep brain stimulation of the ventral intermediate nucleus of the thalamus provides a suitable therapeutic option in tremor dominant movement disorders. However Holmes-tremor, as a condition of traumatic or ischemic origin, still proves to be difficult to manage using conventional techniques. Individual anatomical differences and lesions in various components of neural networks regulating fine movements can contribute to an even more complicated clinical picture.

Methods: 2 patients, a 16 year-old boy and 35 year-old woman, suffering from medically intractable Holmes-tremor were selected for deep brain stimulation. The 16 year-old patient started to develop a right upper extremity tremor 3 months after a car accident. The female patient has started to show signs of a left upper extremity tremor accompanied by a dystonic posture 2 years after a brainstem cavernoma bleeding at the level of the red nucleus. 3D T1 (1x1x1 mm, isotropic voxels), contrast enhanced T1, SWI (0.68x0.68x1.5 mm), and DTI (32 directions, 2x2x2 mm, isotropic voxels) MRI sequences were acquired preoperatively from both subject on a Siemens Verio 3T scanner. DTI analysis has been carried out using FSL 5.0.9 (FMRIB Software Library, Oxford), while cortical parcellation was done using Freesurfer 5.3.0 (Martinos Center for Biomedical Imaging, Harvard University). Subcortical seed regions for probabilistic functional segmentation of the thalamus and visualization of dentate-rubro-thalamic tract were delineated manually. Probabilistic tracking has been carried out using FSL ProbtrackX with default settings and modified Euler streaming. Results of tractography were fused with anatomical T1 images, stereotactic targets were identified on a Medtronic Planning Station running Framelink 5 (Medtronic Inc., Minnesota). For proper lead placement, intraoperative microelectrode recording, macrostimulation, and fluoroscopy were utilized.

Results: Probabilistic tractography was able to visualize the dentate-rubro-thalamic tract in both patients, however, it was only partially traceable in our female patient due the extensive lesion at the level of the red nucleus. Distinct functional subgroups within the thalamus were also identified providing a well estimated location of the ventral intermediate nucleus. Intraoperative microelectorde recording and macrosimulation correlated with the tractography, while tremor was reduced significantly due to microlesional effect and stimulation. Final lead and stimulation contact positions were evaluated on postoperative CT-tractography fusion images showing both leads residing in the ventral intermediate

nucleus, the dentate-rubro-thalamic and thalamo-cortical pathways 6 weeks after surgery.

Conclusion: Using novel imaging techniques, thalamic nuclei and the dentate-rubrothalamic tract can be properly identified. Probabilistic tractography, while identifying important components of the affected neural networks, can provide a safe and viable option in the surgical management of Homes-tremor, resulting in long lasting tremor control.

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#8656

Neuropsychiatric Effects of Deep Brain Stimulation and Levodopa-Carbidopa Intestinal Gel in Advanced Parkinson's Disease

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Keywords: Neuropsychiatric effects, Deep brain stimulation, Levodopa-carbidopa intestinal gel.

Introduction: Advanced Parkinson's disease (PD) is an indication for advanced interventions such as deep brain stimulation in the subthalamic nucleus (STN DBS) or infusion of levodopa-carbidopa intestinal gel (LCIG). Observations regarding neuropsychiatric effects after respective treatment consist of conflicting or insufficient data. Additional knowledge regarding neuropsychiatric effects may help identify appropriate candidates for these treatments.

Aims: To compare the possible differences in neuropsychiatric profile and quality of life (QoL) after intervention between STN DBS and LCIG patients. To determine possible neuropsychiatric effects of respective intervention by comparing neuropsychiatric profiles in respective patient group to controls.

Material and Methods: A cohort of 40 patients with advanced PD, 13 STN DBS, 12 LCIG and 15 controls were investigated. Neuropsychiatric effects were investigated by computer-based assessment of working memory and impulsivity. In addition, values from a depression rating scale and QoL scales were collected.

Results: No significant differences were detected regarding neuropsychiatric profile or QoL in comparisons between STN DBS and LCIG patients ($P > 0.05$). In three group comparisons including the control group, trends towards differences in self-rated QoL were found indicating highest self-rating in LCIG patients and lowest in the controls ($P = 0.054$).

Conclusions: No significant differences between patient groups could be observed. Trends indicating better QoL in patients with advanced treatment were observed. Prospective randomized studies in larger patients cohorts with neuropsychiatric evaluation before and after respective treatment are warranted to fully determine clinical effects of these therapies.

#8747

The Evolution of Cognitive Abilities and Disability in Parkinson's Disease after Ten Years of Subthalamic Deep-Brain Stimulation

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Keywords: DBS, Cognition, Disability.

Introduction: The evolution of cognitive abilities after the deep brain stimulation (DBS) in Parkinson's Disease (PD) is a challenging matter in particular for subjects implanted at the subthalamic nuleus (STN): controversial findings and the fear of a possibly negative impact emerged from the literature that is poor of long-term follow-up studies.

Objective: The primary objective was to follow the evolution of the cognitive abilities and disability after ten years of STN-DBS, through a perspective observational study over ten years of follow-up. Secondarily we studied the relationship between the cognitive evolution and the evolution of disability in this kind of subjects.

Methods: Study design: prospective cohort study with follow-up to 10 years. Subjects with PD were enrolled in the study if they underwent consecutively, since 2005, the high frequency stimulation of subthalamic nucleus bilaterally. Patients underwent an evaluation protocol, before the intervention and annually after implantation, which included disease-specific scales, global and selective clinical monitoring (UPDRS), the structured assessment of cognitive skills, as well as verification of therapeutic window of stimulation parameters and the antiparkinsonian drug therapy. The following tests were used as a cognitive outcome measures: MiniMental State Exsamination (MMSE), Frontal Assessment Battery (FAB), Rey's Test of Words, Corsi's Test (CS), Digit span (DS), Raven Colored Progressive Matrices (RCPM), Attentive Matrix (AM), Trail Making A/B (TM A-B), Stroop Test (ST), Test Weigl (WT), copying designs (constructional praxis-CA), Test of overlapping figures (VST-visuospatial tests), phonemic fluency (PF), semantic fluency (SF); The functional outcome was assessed by UPDRS part II (ADL).

Results: Thirty subjects were enrolled: mean age 60.0 [SD 6.4], years of disease 11.8 [SD3.4], education 7.4 [SD 3.9], UPDRS Section II 15.9 [SD 5.6], LEDD 1055 [SD 353] mg, MMSE 26.5 [SD 3.2], FAB 15.1 [SD 2.9]. After 10 years of follow-up, on average, verbal and non-verbal memory remained unchanged; executive functions (ST, TMB) and fluency worsened significantly ($p < 0.01$): subjects lost 25% word at the SF test and the 19% at

the PF. Ten patient (20%) showed a moderate-severe global cognitive impairment and reached a MMSE score lower than 20/30. UPDRS II showed, in the first 5 years after surgery, a significant improvement, which was gradually reducing until it disappeared and reversed at the tenth follow-up (Chi2 = 30.9, $p < 0.0001$). No direct relation was found between UPDRS II and MMSE after ten year of follow-up.

Conclusion: Subjects with STN-DBS for PD showed a prevalence of dementia similar to that of general PD population, as described in the literature. Also the evolution of the different monitored abilities confirm previous data. Cognitive condition did not emerged as predictor of disability.

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#8762

Successful Combination of SPG and ONS for Cluster Headache

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Keywords: Cluster headache, SPG, Occipital nerve stimulation.

Introduction: Different neuromodulation methods are established to treat chronic headache and several reports indicate that sphenopalatin ganglion (SPG) stimulation offers advantages in Cluster headache over other other stimulation methods as occipital nerve stimulation. Limited evidence exists for both methods regarding both long-term efficacy and mechanism of action. We report on a patient suffering from chronic cluster headache with >20 attacks/months, who partially benefits from ONS and underwent additional SPG stimulation.

Methods: The patients is a 47 y old male suffering from cluster headache therapy refractory to conventional medical treatment. He underwent ONS in another department via a midline approach at the C0/1 level with two octrodes connected with an IPG in the buttock (EonMini, St. Jude Medical). Reported initial reduction in headache days (from 25 to 4 days/months, VAS 10/10 to VAS 4/10) was lost after three months of treatment, when he consulted our department. A dislocation of one electrode was seen and a technically successful revision was performed. However, the patient reported stable conditions after 6 months with 20 headache days per months (VAS 8/10, required up to 60 triptane injections/month). As the patient still remained severely disabled and was unable to work we considered an additional SPG stimulation.

Results: A permanent SPG stimulation device (ATI) on the left side was implanted in collaboration with the ENT department, no adverse events occurred. Stimulation was switched on 4 weeks postoperatively. Using conventional stimulation parameters (120 Hz, 434 µs, 1.6 mA, 1+, 3-), pain relief was achieved with a significant decrease in cluster attacks (6 attacks/months). Additionally a reduction in triptane use to 8 injections per months was noted.

Conclusions: This case report indicates that a combination of different neuromodulation methods to influence the trigeminoautonomic system is feasible, effective and safe.

#8764

Successful High Frequency Burst Stimulation in Refractory Angina Pectoris

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Keywords: Angina pectoris, SCS, Pain.

Introduction: Angina pectoris and neuropathic pain disorders are highly prevalent. Spinal Cord Stimulation (SCS) may provide pain relief in these patients. During SCS treatment, paraesthesia is generally experienced by the patient. The significance of paraesthesia on treatment efficacy, the possible role of placebo effects, and the importance of electrode position are not well understood. However, a significant percentage of SCS patients (~20%) experiences long-term loss of effect ('non-responders'). We report on the effectiveness of a new paraesthesia-free SCS stimulation paradigm (Burst) for the treatment of angina pectoris (AP) refractory to tonic stimulation.

Materials/Methods: A 60 y male patient with a pre-existing 11 y history of severe coronary heart disease, diabetes mellitus, several myocardial infarctions, Bypass surgery, failed PTCA and PVD underwent conventional midline SCS. The tips of the two paramedian octrodes were placed at the Th2 level. After a successful trial period, the permanent stimulator was implanted in the right buttock. (EonMini™, SJM). Preoperatively, the patient suffered from 3–4 VAS 7/10 AP attacks daily.

Results: At the 3 months follow-up we saw a partial effect on the continuous background pain with tonic stimulation (50 Hz, PW 412 µs, amplitude Perception at 5.10 mA, Comfort at 6.80 mA, continuous stimulation) but not on the peak attacks (stimulation left 0 0 + + – – – +, right 3+, 4+, 5–, 6–, 7–, 8+). Since this settings failed to improve quality of life, we decided to test BURST stimu-

lation. A single-blinded allocation for a period of 1 week each was tested: Tonic 30 Hz Stimulation, Burst Stimulation with 500 Hz 1000 µs, and placebo (off) stimulation (burst Frequency 500 Hz, 40 bursts per second, PW 1000 µs, BurstActive 5 (Pulses), Target 70% of 3, cyclic stimulation 3600 sec. on/15 sec. off). The patient reported immediate pain relief under burst stimulation (VAS 1/10), no pain relief in placebo and tonic setting was reported. Pain relief was stable at 6 months follow-up. No stimulation induced side-effects were observed.

Discussion: Two key findings are presented in this study: 1) SCS produces reproducible and reversible pain relief in patients suffering from AP refractory to conventional treatment and 2) paresthesia is not mandatory for effective treatment. SCS is effective both in suprathreshold tonic and high frequency burst stimulation. Burst stimulation might be an alternative for AP cases refractory to tonic stimulation. Further non-inferiority designed studies are ongoing to proof this concept.

Conclusions: Overall, paraesthesia-free Burst Stimulation resulted in better pain relief in this AP patient. These encouraging results form the basis for further investigations.

#8766

Usefulness of Segmented Leads in Anatomical Variants of the Brain

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Keywords: DBS, Segmented leads.

Introduction: Deep Brain Stimulation is an established treatment modality in various movement disorders including dystonia. Due to the close proximity of the most common target point (GPi) to critical functional structures as the optic tract and the internal capsule, therapeutic yield might be limited by side effects.

Recently, segmented DBS leads have been made available. This technique comes with the promise of increased efficacy and side effect reduction. We hereby report on the first case of dystonia treated with directional lead deep brain stimulation.

Methods: A 31 year old female presented with a 20 year history of generalized dystonia. The severe additional ataxic component left her wheelchair bound and she suffered from severe dysarthria. The neurological complex was thought to be caused by a proven isolated Vitamin E deficiency syndrome. MRI revealed structural changes of the basal ganglia anatomy with anatomical distortions pronounced on the left (Image 1). Standard coordinates did not match the individual anatomy of the patient. She therefore underwent bilateral GPi DBS surgery using direct targeting of the left GPI. Directional leads were implanted in both hemispheres.

Results: After calculation of standard AC-PC coordinates (3.5 mm anterior, 22.0 mm lateral and 4.0 mm below MCP) the trajectory was adapted guided by MRI anatomy to the lateral border of the optic tract. The posterior communicating artery took a atypical course above the optical tract further limiting the approach. Targeting was guided by three micro electrode recording tracts and a directional lead system (Vercise DBS, Boston Scientific) was implanted in an all-in-one GA setting. Conventional stimulation caused a fast worsening of the dysarthria and painful stimulation induced side effects. The segmented contacts were intensively tested at 90 µs and 130 Hz in the postoperative course. Distinct effect/side-effect patterns for each contact were observed.

Conclusions: Segmented leads allowing current steering offer new perspectives for DBS and will likely result in increased treatment efficacy while reducing side effect at the same time. While this is true for well known disorders and their targets (PD, generalized dystonia) this technique also yields the potential to treat disorders currently not amendable to DBS as no good benefit/side-effect ratio could be achieved with conventional DBS. This includes diseases as described here with complex and basically unknown changes in basal ganglia functionality and structure.

#8771

High-Frequency Spinal Cord Stimulation in Surgery-Naïve Patients – A Prospective Single-Center Study

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Keywords: Lower back pain, SCS, High frequency stimulation.

Introduction: A multitude of evidence supporting the beneficial effects of spinal cord stimulation (SCS) in patients suffering from chronic pain syndromes following spinal surgery has been published in the last decade. Evidence is scarce however for the use of high frequency SCS (HFSCS) in the treatment of surgery naïve patients suffering from lower back pain (LBP).

Methods: From June 2014 to April 2015 we prospectively enrolled patients suffering from LBP alone or in conjunction with leg pain in a trial of HFSCS. None of the patients had undergone surgical procedures of the thoracic, lumbar or sacral spine. Patients suffered medically intractable LBP and were deemed ineligible for spine surgery due to mismatches in imaging findings and clinical symptoms, or were medically unfit to undergo extensive surgical procedures. All patients underwent trial stimulation for at least one week. IPG implantation was conducted only following successful trials. Pain levels were assessed daily during initial stay, 4 weeks later and then every 3 months. Different pre-programmed modes of HFSCS were changed if pain persisted or increased during trial or post-implant follow-up.

Results: A total of 8 patients (4 male, 4 female) underwent HFSCS trials. Mean age was 60 ± 4.8 years. Mean VAS baseline intensity for back pain was 8.9 ± 0.23 and 8.1 ± 0.6 for leg pain. All patients achieved meaningful reductions in pain intensities and underwent IPG implantation at a mean interval of 13 ± 1.3 days. Mean follow-up was 306 ± 48 days in February 2016. Mean back pain VAS reduction from baseline at last follow-up was –4.13 ± 0.85, and –6.2 ± 1.03 for leg pain. Two patients showed skin irritations and localized pain at the IPG site. Both patients underwent

surgery to replant the IPG. No infections were seen in any of the 8 patients enrolled.

Conclusions: In this prospective cohort of surgery naïve patients we were able to show good efficacy of HFSCS for both back and leg pain. Reductions were long-lasting with a mean follow-up of nearly 10 months in our cohort, and a mean VAS reduction at last follow-up of 4.13 and 6.2 for back and leg pain, respectively.

#8798

Functional and Painful Pudendal Syndrome: Outcome with Pulsed Radiofrequency as First Treatment Step

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Keywords: Pelvic pain, Pudendal syndrome, Pundenal neuralgia, Sphincteric disfunction.

Background: The Pudendal Nerve Neuralgia is a cause of chronic pelvis pain in both male and female. This pain is distributed in the pudendal nerve territory and can affect all function of this nerve (sensory, motor and autonomic). The causes are classified in primary or secondary (in this case is related with history of trauma, abdominopelvic surgery, radiotherapy, etc.) The diagnosis and treatment of this condition is a challenger, due the variety of clinical presentation, the delay in the diagnosis and the lack of evidence in which is the best treatment options, attempt directly in the cure of this syndrome.

Objective: The aim of the study is to analyze the outcome of the pulsed radiofrequency in our patients with Pundendal Syndrome and determine possible factors related with the best following treatment election.

Materials and Methods: Retrospective analysis involving patients with pudendal neuralgia treated with pulsed radiofrequency by the Department of Neurosurgery, Italian Hospital de Buenos Aires, since June 2015 to December 2015. The radiofrequency was performed to all patients as first step for diagnosis and treatment. Previously, the patients had to fill Pelvic Pain and Sphincters Disorders Form, performed by the Center Pelvic Pain and Sphincters Disorders of the Italian Hospital in concordance by the International Pelvic Pain Society. These guide assesses all aspects of this kind of syndrome (pain aspects and Sphincters function). Then relevant data were collected and analyze. We excluded all patients that not accomplish the Nantes's Criteria. We used de Visual Analogue Scale (VAS) to assess the pain.

Results: A total of twenty patients were treated in this period, thirteen were woman (65%) and seven were men (35%). The average age was 51.6, with a range between 31 to 74 years. The clinical history background is different between sex: urological background with 61.53% in women (interstitial cystitis, urethroplasty, reiterative urinary infection) and 85.71% in men (chronic prostatic infection, prostate resection, radiotherapy); coloproctological with 38.4% in woman (rectal prolapse, colostomy, enterocele); and gynecological 46.15% (utheropexy, structural pelvic pathology, etc.). The average time between the onset to symptoms and the first consult was 28 months, with a range between 5 to 120 months. All patients complained for pelvic pain according Nantes Criteria in the first consult, except one that the syndrome was Sphinteric pure at the onset (affecting the defecation) and then appeared the pain aspects. The average VAS previous (VASpr) the treatment was 8.52, with a range 3 to 10. The pain was associated with sphinteric dysfunction in 8 patients (40%), characterized with combined affections in 50% (urologic and coloproctological) and isolated urinary or coloproctological symptoms both with 25%. The outcome was assessed with VAS: in the first cycle of radiofrequency, the VASpr decrease in 41%. In the second cycle (VAS2), the VAS decrease in 60.1% and 43% if it is compare with the VASpr and the VAS post first radiofrequency respectively. Finally, the VAS in the third cycle decrease in 34% and 35% if it is compared with de VASpr and VAS2. The sphincter function improved in 6 of 8 patients, more frequently in urinary symptoms.

Conclusion: The pulsed radiofrequency is a very efficient treatment of the symptoms derived of pudendal neuralgia. In consequence of the lack of information in the literature related with the effectivity, is recommended a series from 2 to 4 procedure in every patient despite the partial improvement, separated with 2 o 3 months between it. In our series we notice that the best improvement was in the second cycle compared with the others. Some features of the clinical history of the patient like the background of trauma, the isolated pain in the penis, the time from the symptoms onset until the first consult more than four years, the poor response to opioids, could be special factors to consider in the election of the amount of radiofrequency cycles and the necessity to pass to the next step in the treatment protocols.

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#8802

Therapeutic Susceptibility of Head Tremor in Patients Affected by Essential Tremor after Unilateral Thalamotomy of the Drive Side with MRgFUS

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Keywords: MRgFUS, Head tremor, Lesion.

Axial tremor is detected in 40% to 60% of patients affected by Essential Tremor (ET). Head tremor, when present, severely affects the social aspects and it is recognized as strongly enabling. In respect to tremor of extremity, axial tremor shows lower response to medical treatments and also Deep Brain Stimulation (DBS) of the Ventral Intermedius Thalamus (VIM), even when bilateral, gives inconsistent results. Here we report our preliminary experience in two cases of head tremor successfully treated with MRI-guided focalized ultrasounds (MRgFUS). In April 2016, two men of respectively 35 and 52 years, affected by ET with head tremor underwent unilateral thalamotomy with MRgFUS at our Institution. A previous multidisciplinar (neurological, neurosurgical, psychiatric and anestesiological) evaluation was performed. Screening CT and MRI brain scan with opportune protocols for the visualization of basal ganglia and of the thalamus gave the elegibility to the treatment. The entity of tremor and the relative psychological impact were quantified by la *Fahn-Tolosa-Marin Tremor Rating Scale (FTM)* and *Quality of Life in Essential Tremor (QUEST)*. The baseline FTM score was 38 and 44 respectively. FTM score for head tremor was 4 and 2. The thalamus treated corresponded to the drive side (the more affected one) that was the left for the first patient and the right for the latter. Both patients showed immediate benefit from the procedure, without any side effect. A brain MRI scan with contrast medium excluded complications related to the treatment. Surprisingly, together with the expected disappearance of the extremity tremor, we also observed a strongly relief in axial head tremor that passed to a score of respectively 1 and 0 after the treatment. Unilateral thalamotomy with MRgFUS is efficacious not only to abolish contralateral extremity tremor but it has also a significant impact in ameliorating the axial tremor when the drive side is treated. Even with preliminary observations with limited follow up, this non invasive and high precision technique seems to offer other new perspectives also for other clinical variants of ET, highly enabling and, up to now, not responsive to the traditional therapeutic tools.

#8822

Prevalence of Twiddler's Syndrome May Be Higher in the Internal Pulse Generators Harboring One Anchoring Hole Than Two Anchoring Holes

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Keywords: Twiddler syndrome, Deep brain stimulation, Hardware related complication.

Introduction: Twiddler syndrome (TS) is described as a spontaneous rotation or intentional external manipulation of implanted cardiac or occasionally deep brain stimulation (DBS) devices (1,2). The predisposing factors for development of TS include advanced age with more loose subcutaneous tissue, adipose patients with thick tissue layer precluding proper immobilization of internal pulse generator (IPG), creation of excessively large pocket or obsessive-compulsive behavior (3,4). Additional factor related to the construction of the implanted hardware itself may be the number of anchoring holes in the IPG.

Methods: A prospectively collected database of all hardware related complications for patients operated on at the Neurosurgical Department of Postgraduate Medical Center of Warsaw was performed. In a total number of 347 leads implanted in 211 patients since 1999 we have identified 3 patients diagnosed with TS. All 3 patients with TS in our series were implanted with the IPG harboring one anchoring hole. This complication did not occurred in patients with the IPG harboring two anchoring holes.

Results: All 3 patients underwent revision surgery. During reoperations all IPGs were replaced and sutured with one additional silk suture through the plastic housing of the IPG to immobilize it properly in subcutaneous pocket. There were no recurrences of TS in our patients. All patients gained the previously derived benefit from STN DBS.

Conclusions: Our case series suggests that a predisposing factor of TS may also be the construction of IPG itself (one anchoring hole intended for fixation) which naturally represents less fixation of the IPG to the fascia or muscle in the subcutaneous pocket. This preliminary report may favor the IPG with two anchoring holes which is less prone for development of TS. Placing additional silk suture that pass through a plastic housing of the IPG may help better immobilize the IPG and reduce the occurrence of TS.

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#8823

Pallidal Deep Brain Stimulation in the Treatment of Meige Syndrome

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Keywords: Meige syndrome, Bilateral pallidal stimulation, Deep brain stimulation.

Introduction: Meige syndrome (MS) is characterized by blepharospasm, facial, oromandibular, and cervical dystonia. The medical treatment of this condition is challenging and unsuccessful over long time. Recent case reports and small clinical series showed that bilateral deep brain stimulation (DBS) of globus pallidus pars interna (GPi) improves dystonic features of MS validated by Burk-Fahn-Marsden Dystonia Rating Scale (BFMDRS) (1–5).

Methods: We report on our experience in using bilateral GPi DBS in 5 cases of MS. We present short-term (3 months) follow-up as well long-term (from 24 months to 48 months) results. Preoperative and postoperative BFMDRS assessments were performed on each patient. The postoperative BFMDRS scores was done when both stimulators were switched on and compared to baseline scores.

Results: Bilateral GPi DBS reduced the BFMDRS total movement score by 75% at short-term follow-up, and by 87% at long-term follow-up when compared to baseline scores. The BFMDRS total disability score was reduced by 46% at short-term follow-up, and by 56% at long-term follow-up when compared to baseline scores.

Conclusions: Our results showed that bilateral GPi DBS in MS is effective and safe, if conservative treatment options failed. The benefit is not only observed at short and at long-term follow-up ranging from 24 to 48 months.

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#8824

Deep Brain Stimulation of the Internal Globus Pallidus for Disabling Haloperidol-Induced Tardive Dystonia. Report of Three Cases

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Keywords: Tardive movement disorders, Tardive dystonia, Pallidal stimulation.

Introduction: Tardive dystonia (TD) represents a side effect of prolonged intake of neuroleptic drugs. TD can be a disabling movement disorder persisting despite available medical treatment. Deep brain stimulation (DBS) has been reported successful in this condition although the number of treated patients with TD is still limited to small clinical studies or case reports [1–5]. In this study, we present 3 additional cases of patients with results of bilateral globus pallidus internus (GPi) stimulation.

Methods: The formal assessment included the Burke-Fahn-Dystonia Rating Scale (BFMDRS). The preoperative and postoperative functional and motor parts of BFMDRS were compared in each patient.

Results: Three patients underwent successful bilateral GPi DBS for TD. The postoperative BFMDRS motor score improved by mean of 71% at the last follow-up. There were no surgical or hardware-related complications over follow-up period.

Conclusion: Our experience indicates that bilateral GPi DBS can be an effective treatment for disabling TD. The response of TD to bilateral GPi DBS is very rapid and occurs within days after the procedure.

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#8842

The Human Globus Pallidus Internus Is Sensitive to Rewards – Evidence from Intracerebral Recordings

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Keywords: Globus pallidus internus, Deep brain stimulation, Reward, Oscillations, Local field potentials.

The globus pallidus internus (GPi) is the final output relay of the basal ganglia for the control of movements but has also been shown to belong to a second pathway projecting to the lateral habenula. This latter pathway is related to reward processing. This prompted us to record, in eight patients receiving deep brain stimulation of the GPI for the alleviation of movement disorders, local field potentials while these patients performed a lottery task. The task entailed choosing between a higher and a lower number, which changed their color after the patient's choice with red (green) signaling a loss (win, in Euro cents) corresponding to the chosen number. Surface recordings showed a feedback related negativity from a frontal midline site, while time domain averages in the GPI showed differential modulation depending on the valence of the stimulus with polarity inversion indicating that this reward-modulated activity was indeed generated locally. Furthermore, wavelet decomposition of the LFP showed a reward-related response in the high beta/low gamma range. We conclude that human GPI is involved in reward processing, possibly in relation to the lateral habenula.

#8843

Stable Symptom Improvement after Battery Depletion in a Patient with Deep Brain Stimulation for Secondary Dystonia

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Deep brain stimulation (DBS) has become an accepted treatment for primary generalized and segmental as well as secondary dystonia. Growing evidence of sustained clinical benefit of DBS in dystonia has been reported in long-term studies >10 years. Detailed analysis of reappearance of dystonic symptoms after switch-off has shown rapid restoration of phasic elements within seconds whereas tonic symptoms re-emerged with some delay. It remains unclear, however, whether dystonia will recur in a similar fashion upon longterm DBS.

We report on a 32-year-old patient with generalized secondary dystonia with choreatiform movements due to perinatal asphyxia. The pre-operative Burke-Fahn-Marsden Scale motor score (BFM) was 80.5, disability score (DS) 19. Six months later, implantation of quadripolar stimulation electrodes (Model 3387; Medtronic Inc., Minneapolis) was performed bilaterally in the ventral intermediate nucleus (Vim) of the thalamus as well as the posteroventral lateral GPi with CT-guided stereotactic surgery and microelectrode recording. Post-operatively, the patient showed sustained improvement of the dystonic tremor and fine motor skills, he was able to grip objects and could guide the glass to his mouth by himself. Furthermore his speech improved (BFM 67.5, DS 15 at 17 months postoperatively).

Eventually, at 76 months, our patient presented for his routine follow-up and reported, that his DBS might have switched off. IPG check revealed a battery at end of life and analysis of DBS activity displayed an off-switch 5 weeks ago. Clinical examination was stable (BFM 69, DS 15).

Our patient had sustained clinical benefit as reflected by stable BFM score, which goes beyond the observations of improved symptoms after DBS discontinuation compared to the pre-OP situation. In parallel to previous reports he was under DBS for long time. To our knowledge, this is the first case of sustained therapeutic effect of DBS in dystonia after battery depletion in secondary dystonia. Systematic studies need to be performed to assess such neuromodulatory effects.

#8846

The Spinal Cord Stimulation to Patients with Pain and Spastic Syndromes

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Keywords: Spasticity, Chronic pain, Myelopathy.

Objective: One of the most important problems of today's neurosurgery and neurology practice is strict patient selection for spinal cord neurostimulation. For this purpose it is very important to define the character and the power of pain and the level of the muscle tone, to analize the results of stimulation electromyography and to implant the trial system before operation.

Matirial and Methods: SamaraRegionalHospital neurosergery department use spinal cord stimulation systems implanting in the posterior epiduralspaceto patients with pain and spasticity (muscle spasm, spastic limbs) as a part of a complex therapy. 41 patients have been operated: 12 women and 29 men with there age ranging from 22 to 63 years. In 12 cases there was an injury of cervical region, in 23 cases – thoracic region and in 6 cases – lumbar region of the vertebral column. The electrode was implanted in the posterior epidural space on the lumbar level by a standard procedure.

Results: The result of neurostimulation is improvement of the quality of life of the patients (using the SF-36 survey): pain relief for 55–60%, muscle tone decreasing – from 2.85 to 1.35

points, what is confirmed by the results of stimulation electromyography.

Conclusion: The results of spinal cord stimulation depend on strict patient selection. After operation patients with chronic pain and spasticity find that neurostimulation positively impacts the quality of their lives: they achieve reduction in pain and decreasing of muscle spasm in limbs. Patients find that they can decrease or stop taking painkillers or other pain medications, they return to a more normal lifestyle and normal activities, aphysical therapy program recommended for them becomes more various.

#8849

Optimization of Deep Brain Stimulation by Means of a Patient-Specific Mathematical Model

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Keywords: Deep brain stimulation, Computer modeling, Optimization.

Deep Brain Stimulation (DBS) is an established treatment in neurological diseases, e.g. Parkinson's disease or essential tremor (ET), while its underlying biological mechanisms are still have to be elucidated. DBS consists of delivering electrical pulses to a target in the brain through implanted electrodes. It is believed that maximal therapeutic outcome is achieved when the target is completely stimulated while the stimulation beyond it is kept as small as possible, thus minimizing the risk of side effects. To facilitate this goal, recent developments in DBS leads enable asymmetrical stimulation with segmented contacts. The field produced by the lead can then be shaped more accurately, limiting the spill to adjacent areas.

Due to the limitations of *in vivo* studies, mathematical models aiming at a better understanding of DBS have been developed in the past years. In order to correctly predict the stimulation spread, the model has to take into consideration the patient-specific brain anatomy. In particular, white matter, grey matter, and cerebrospinal fluid possess different electrical properties. This can be taken into account by using Magnetic Resonance Imaging (MRI). Then, a Finite Element model individualized to the patient can be created. The stimulation field spread is optimized so that it completely covers a certain target that is manually segmented from MRI. In this case, the criterion for distinguishing between stimulated and non-stimulated domains is an electric field threshold of 200 V/m.

However, when individualizing the model, two uncertainties exist: the actual position of the lead and the reaction of the brain tissue to the implanted electrode. The lead position is estimated from an image obtained by post-operative Computer Tomography. However, the estimate accuracy is comparable to the size of the target, i.e. a few millimeters, and has to be accounted for in the stimuli optimization. Animal studies suggest that an encapsulation layer is formed around the lead after the surgery. *In vivo* impedance measurements in the human as well signalize this possibility.

The developed model has been applied to a clinical case of stimulating the caudal Zona Incerta in an ET patient with a segmented lead. The obtained stimuli optimization results agree well with symptoms observation.

The mathematical model of DBS is expected to be useful in e.g., shortening the programming time and/or reducing possible discomfort to the patient. In addition, potential gains of using alternative lead designs can be tested *in silico* in an inexpensive and prompt way.

#8853

Characterization of Pre- and Post-Weaning Behavior in a Rodent Model of Depression: Early Affective Dysfunction Reflected in Vocalization

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Keywords: Model of depression, Rat, Vocalization, Early phenotype.

Introduction: Ultrasonic vocalizations (USV) are used by rats in a context and state dependent manner and can considered as an index of their psychological state as calls within specific frequency ranges are associated with distinct affective categories such as fear and anxiety (negative emotions, 20–30 kHz band), or playfulness and mating (positive emotions, 40–60 kHz band). The current study examined post-natal vocalization in the Flinders Sensitive Line (FSL) rodent model of depression, including the value of early vocalization in predicting subsequent behavioral deficits. Follow-up studies will investigate the behavioral and biological impact of Medial Forebrain Bundle High Frequency Stimulation in this model.

Methods: Flinders Sensitive Line (FSL) and age and gender matched Sprague-Dawley (SD) control rats derived from the breeding colony in the animal facility of the Freiburg University Medical Center were used. A total of 31 FSL and 39 SD pups were tested from 4 FSL and 3 SD dams, respectively. Behavioral assessment started on post-natal day 3 and continued until the age of 13 weeks. The pups were weaned at day 28 and perfused at age of 14 weeks.

Results: Pre-weaning FSL pups (post-natal days 3–21) emitted significantly fewer calls compared to control rats. Following weaning (from week 4), FSL continued to vocalize less until week 8, and the reduced number of calls affected specifically the 40–60 kHz band. The young adult FSL rats also showed increased depressive-like behavior in the Forced Swim Test.

Conclusions: FSL pups have depressive phenotype already during the first few weeks post-natally, as manifested by the overall reduced vocalization, and particularly in the positive affect spectrum. The pre-natal developmental/biological factors and the environmental ones – such as reduced maternal attention during the post-natal period, need additional investigation.

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#8854

Subthalamic Nucleus Deep Brain Stimulation Does Not Affect Language and Cognitive Abilities of Greek-Speaking Individuals with Parkinson's Disease

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Keywords: Cognitive abilities, STN DBS, Parkinson's disease.

Introduction: The evidence regarding the impact of subthalamic nucleus deep brain stimulation (STN-DBS) on language and cognitive abilities of individuals with Parkinson's disease (PD) is contradictory. Moreover, the bulk of the evidence is based on English, a morphologically poor language. STN-DBS has recently been found to compromise the rule-based past tense formation in English.

Methods: Language tasks tapping rule-based past tense formation and comprehension of relative clauses and cognitive tasks tapping short-term memory, verbal working memory, set-shifting, and inhibition were administered to eight non-demented PD speakers of Greek, a morphologically rich language. Three participants were assessed before and after STN-DBS (Testing Type 1), and five participants with the stimulator on and off (Testing Type 2).

Results: No indication of deterioration in any of the language and cognitive abilities was detected after DBS or during stimulation. On the contrary, in Testing Type 1, one participant benefitted from STN-DBS in comprehending one type of structurally complex sentences and in inhibition, and another one benefitted in inhibition and set-shifting. In Testing Type 2, all tasks elicited similar performances across stimulation conditions both at the individual and group levels.

Conclusions: The results suggest that STN-DBS does not affect cognitive and language abilities of Greek-speaking PD individuals. (The sporadic benefits observed in Testing Type 1 can be considered a pre-surgery stress-related artifact.) Language-specific properties, such as morphological/inflectional richness, may determine the impact of STN-DBS on morphosyntactic processes. Rule-based past tense formation, for example, may not be affected in highly inflected languages.

#8855

Olfactory Memory Deficits in the Flinders Sensitive Line Rodent Model of Depression

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Keywords: Model of depression, Rat, Anosmia, Olfactory discrimination.

Introduction: Major Depressive Disorder (MDD) is a heterogeneous psychiatric disorder with broad symptomatic manifestations impacting on many facets of the sufferers' life. Typically it is associated with anhedonia, loss of interest in most activities, feeling of despair, pervasive pessimism about the future, suicidal tendency, and anosmia. The current study examined state of olfactory memory and discrimination in the Flinders Sensitive Line rodent model of depression. Follow-up studies will investigate the behavioral and biological impact of Medial Forebrain Bundle High Frequency Stimulation in this model.

Methods: Male Flinders Sensitive Line (FSL) rats and Sprague-Dawley (SD) controls were trained on an Olfactory Discrimination test and a Social Interaction test to permit the evaluation of olfactory memory and discrimination, but also the drive to explore novel scents.

Results: On the Olfactory Discrimination test, the FSL and the control animals performed similarly at the shortest inter-trial interval (5 min) confirming that FSLs can learn and discriminated between known and novel odors. However, with extended delay of 30 min, the FSLs had a robust recall and odor discrimination deficit. At the longest delay (60 min) both groups performed equally poorly. The Social Interaction test further confirmed that the FSLs are less likely to explore and interact with an unfamiliar rodent.

Conclusions: The FSL rats, compared to the controls, showed a robust deficit in olfactory discrimination suggesting an impairment in olfactory memory and recall. FSL were also less likely to socialize with novel rats. Taken together, the data suggests that the FSL animals might have an impaired olfactory information processing capacity, or less motivated to explore novelty, both indicating potentially a dysfunctional limbic system.

#8866

Dynamics of STN Low-Frequency Components Upon DBS

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Keywords: DBS, Parkinson's disease, PD neural markers, STN rhythms.

Introduction: Deep brain stimulation (DBS) of the subthalamic nucleus (STN) has developed into a standard therapy for treating refractory stages of Parkinson's disease (PD). DBS systems nowadays represent open loop technology. DBS is applied to the target area, without taking into account the motor state of the patient. Despite being a widely accepted approach, continuous and chronic DBS (cDBS) is suspected to cause side-effects such as speech impairment or tolerance to treatment, and has disadvantages with regard to energy efficiency and battery life [1, 2]. It would be desirable to have adaptive DBS (aDBS) systems, which provide stimulation on-demand only and which reduce or stop stimulation during sleep or other periods of inactivity. To realize the closed loop control of a patient's motor symptoms by an aDBS approach, information about the motor state of the patient is required. Besides recordings of the actual motor output, such information may be provided by neural markers [1, 3, 4]. The power of LFP oscillatory components in the beta range (12–30 Hz) recorded from basal ganglia is considered the most informative neural marker. However, even lower frequent oscillations have been reported informative about dyskinetic symptoms [5]. As brain processes are highly non-stationary, the dynamics the neural markers and dynamic effects that DBS has on them should be considered [6] in the context of aDBS. In the present work, investigate dynamics of the theta power upon DBS.

Materials, Methods, and Results: Intraoperatively micro-electrode recordings (MER) were acquired as part of the implantation procedure for DBS of four PD patients (S1-S4). In each hemisphere, three electrodes were lowered into the target region STN simultaneously (anterior, central, lateral) over a Ben's gun approach (FHC, USA). Stimulating on a singular macro-tip of the telescopic FHC electrode (FHC, USA) with increasing currents allowed to record signals with 5 kHz sampling rate from two other MER positions (Leadpoint, Medtronic, USA). Starting with stimulation *off*, stimulation intensity was ramped up in steps of 0.2 mA and 0.5 mA. Each intensity was delivered for 10 s at a rate of 130 Hz with interleaved pauses of 20 s duration to allow a washout of the DBS effects. During the ramp-up tests, patients were asked to neither move nor speak in order to avoid artifacts and spurious effects.

For S1, analysis of the left-hemisphere data had to be omitted due to acquisition issues. For the offline analysis of the remaining data, the first 15 s of the interleaved pauses (stimulation-off intervals within the ramp-up sequence) were extracted after bandpass filtering the data between 2 Hz and 8 Hz. Subsequently, the envelopes of the band-filtered signals were extracted by computing the real part of the Hilbert transformation of the data. Results are reported per subject and hemisphere. Within each hemisphere, the effects are average over all the stimulation-off intervals of a ramp-up sequence.

For at least five out of the seven analyzed data sets we observed a desynchronization within the first 5 seconds after stim off in at least one of the two recorded electrodes. Observed envelope effects are not necessarily comparable between hemispheres of a subject, probably because the exact location of the recording electrodes within the STN areas varies.

Conclusions: Beta-band oscillations are referred to as the most important neural marker for assessing effects of DBS in PD-patients. We have shown that other neural oscillations also react upon DBS, specifically theta-rhythms [2–8] Hz. Our data suggests, that the time dynamics should be considered if theta activity is exploited in aDBS approaches.

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#8877

Impact of Segmented Leads for DBS

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Keywords: DBS, Segmented leads, Current steering.

Introduction: Deep Brain Stimulation is an established treatment modality in various movement disorders. Targets are usually located within the basal ganglia. Due to the proximity of the target points to critical functional structures as the internal capsule, therapeutic yield might be limited by side effects. Furthermore energy consumption is potentially higher in conventional monopolar stimulation. Recently, segmented DBS leads have been made available. This technique comes with the promise of increased efficacy and side effect reduction. We therefore compared our preliminary data with segmented leads with the data from the Libra study conducted 4 years ago.

Methods: The purpose of the Libra study was to evaluate the effects of a new Deep Brain Stimulation System for reducing symptoms of advanced, Parkinson's disease Also the Activities of Daily Living, UPDRS scores, Quality of life of subject, device parameters including active contact in relation to efficacy, frequency,

type and severity of therapy related AE's events were evaluated. 3 months data from patients with segmented leads (Infinity) 6 patients will be compared to the Libra data (6 patients).

Results: DBS Targeting was guided by three micro electrode recording tracts and a directional lead system (Infinity DBS, SJM) was implanted in an all-in-one GA setting in 6 patients. The segmented contacts were intensively tested at 90 µs and 130 Hz in the postoperative course. Distinct effect/side-effect patterns for each contact were observed. Comparison of Parkinson's symptoms as demonstrated by the UPDRS motor scores in the medication 'off' state at Baseline compared to the medication 'off' with stimulation 'on' 3 months after device implantation. No differences in efficacy where seen between Libra and Infinity data amoing those 6 patients. However compared to the Libra data, no stimulation dependent side effects occurred in the Infinity group. Amplitude and frequency did not differ, however lower pulse width was used in 2 patients.

Conclusion: Segmented leads allowing current steering offer new perspectives for DBS and will likely result in increased treatment efficacy while reducing side effect at the same time. While this is true for DBS in general, there are cases with no good benefit/side-effect ratio could be achieved with conventional DBS. Since the threshold for side effects is higher in segmented leads, they are more adaptable to the individual patients needs and potentially resulting in a longer battery life.

#8879

First Experiences with Directional Leads for DBS in Parkinsons Patients

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Keywords: DBS, Directional leads, Parkinsons disease.

Introduction: DBS has been etsablished for the treatment of movement disorders and many other diseases within the past 2 decades. One of the most popular target areas for DBS in Parkinson's disease (PD) is the area of the subthalamic nucleus. Whereas the overall effects of conventional DBS lead to significant improvement of the cardinal smyptoms of PD, there may be some limits, especially, if the electrodes are too close to some of the neigbouring structures, such as the internal capsule. The stimulation parameters sometimes may have to be reduced because of side effects in these cases, such like dysarthria, spasticity and similar ones.

Methods: Very recently, a new system had been relaesed for DBS in PD patients with the possibility to direct the current in certain directions, while suppressing others. This is beeing achieved by a segmentation of the electrodes. We report about our first, still limited experiences with this type of Deep Brain Stimulation device in 6 patients with PD. all patients underwent conventional preoperative testings according to the brain bank criteria and also the planning and targeting, as well as the intraoperative testing was performed in the conventional way; awake surgery with intraoperative microrecording and macrotesting. CT/MRI matching for the planning of the procedure.

Results: All patients were bilaterally implanted and had a significant success due to the DBS implantation. While intraoperatively sufficiently tested, 2/5 patients required adaptations of their stimulation parameters postoperativeley leading to capsular side effects with conventional stimulator settings.

In both patients, through the activation of the electrode segmentation, leading to directional steering of the stimulation current, allowed us to increase the stimulation current without capsular side effects. Both patients improved afterwards due to their PD symptoms. Videos with different stimulation parameters (with/out) directional current steering will be shown.

Discussion: Directional current steering provides new and potentially helpful options for DBS treatments. However, the indications for this special kind of DBS may vary due to different indications and different target ares.

#8888

Rechargeable Pacemaker Technology in Deep Brain Stimulation: A Step Forward, But Nor for Everyone

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Keywords: DBS, Rechargeable, Pacemaker.

Objective: Since a few years rechargeable pacemaker technology is available in deep brain stimulation. This technical innovation becomes more and more important in our clinical practise, particularly for patients with high amplitude and accordingly high wattage. But due to the requirements in handling the rechargeable device, this kind of pacemaker is not eligable for every patient.

Methods: Over a period of ten years around 360 patients underwent deep brain stimulation for several indication in our department. Rechargeable pacemaker are often used for replacement after battery depletion or sometimes for first implantation. Within this time for two patients we had to change the rechargeable pacemaker against a non-rechargeable one before its actual expiration of term because of difficulties with the application.

Results: First patient is 73 years old with Parkinson's disease, underwent bilateral deep brain stimulation in the internal globus pallidus in 2006. Pacemaker has been changed against non-rechargable ones because of battery depletion in 2008 and 2010. In 2012 it has been decided to implant a rechargeable device because of the comparatively more frequently need of pacemaker-replacments. At the request of the patient in 2014 the pacemakes has been changed against a non-rechargeable one again because of increasing problems with the handling of the recharger and inconvenience with the daily monitoring of the battery level.

Second patient is 62 years old and underwent bilateral deep brain stimulation in the Nucelus accumbens because of an addictive disorder in 2009. The pacemaker has been changed in 2013 against a rechargeable device. In 2015 the pacemaker needed to be

replaced by a non-rechargeable on again. The patient had rising difficulties in coping with the recharging process.

Conclusions: Rechargeable pacemaker are a step forward in providing medical treatment in standard of technical innovation. Many patients stand to benefit from rechargeable pacemakers, smaller devices and less operations. But with the new technology we have new requirements in the technical capabilities and compliance of our patients aswell. Some of them seem not to be up to it or to prefer the simpleness of a non-rechargeable pacemaker.

#8890

Reward Processing Modulates Subthalamic Beta Band Activity in Patients with Parkinson's Disease

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Keywords: Parkinson, STN, Beta band activity.

Tonic dopamine levels modulate the power of beta oscillations in the subthalamic nucleus. The physiological role of this relationship, however, remains unclear. Phasic changes in dopamine may be caused by rewards. Here, we investigated whether beta activity might therefore be related to reward processing. We recorded local field potentials (LFPs) from the subthalamic nuclei of 19 patients with Parkinson's disease who performed a computer-based reinforcement-learning task. Afterwards, we correlated the magnitudes of patients' obtained rewards with task-related power changes in their LFP oscillations. During reward presentation, beta activity was positively correlated with reward magnitudes. During responding, moreover, alpha and low beta activities were negatively correlated with previous reward magnitudes, while the likelihood of repeating the previous response correlated positively. Our results thereby suggest a role of beta activity in the processing of rewards, while alpha and low beta activity might be involved in reward-based response adaptation.

#8894

Hyperkinesias after Long Term Pallidal Stimulation for Dystonia

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Keywords: Dystonia, Hyperkinesias, DBS.

Objective: The globus pallidus internus (GPi) is regarded as an established and safe target for deep brain stimulation (DBS) in dystonia. Recent reports on the occurrence of bradykinetic symptoms like freezing, postural instability and micrographia after chronic DBS of the GPi in patients with dystonia however stimulated a discussion on alternative targets. Here, we report on the unusual occurrence of dyskinesias upon chronic pallidal stimulation.

Methods: A 74-year-old man with segmental dystonia including blepharospasm, orofacial dystonia and aerophagia underwent bilateral stereotactic implantation of DBS electrodes in the GPi. Eleven years later during effective chronic DBS for dystonia he experienced gradual onset of hyperkinetic involuntary movements mainly concerning his arms but also his trunk.

Results: Detailed assessment in various conditions showed that off DBS resulted in an increase of both choreatic hyperkinesias and dystonia. High frequency and low amplitude DBS improved both dystonia and hyperkinesias, while high voltage DBS resulted in further improvement of dystonia but also in increased hyperkinesias. As a compromise between optimal stimulation for dystonia and hyperkinesias we finally choose a bipolar intermediate amplitude stimulation mode.

Conclusion: Chronic pallidal DBS might be accompanied not only by bradykinetic symptoms but also in the rare case by hyperkinesias. Such an occurrence requires complex reassessment of stimulation programming.

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#8895

Complications of Deep Brain Stimulation for Secondary Dystonia in the Early Postoperative Period (30-Day Morbidity): an Experience in 49 Patients

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Keywords: DBS, Dystonia, Complications.

Objective: Deep brain stimulation (DBS) has been shown to be efficacious in the treatment of primary dystonia. There is less experience in secondary dystonia. Since patients with secondary dystonia, who are often more disabled, may be more vulnerable to postoperative complications we aimed to investigate the 30-day morbidity in a large cohort of patients with secondary dystonia operated over a period of 19 years.

Methods: From 1997 until 2016, a total of 49 patients (27 women and 22 men; mean age 43.5 years (range 13–77)) with secondary dystonia underwent DBS with electrodes implanted either in the Thalamus or the posteroventral lateral globus pallidus internus (GPi). Most frequent cause of for dystonia was cerebral palsy in 17 patients.

Results: There were no intraoperative or directly postoperative complications related to surgery. The electrode location was corrected in 2 instances. Two patients developed a wound infection, one patient had subdural hematoma and subcutaneous collection of cerebrospinal fluid (CSF). Three weeks after DBS a subdural hematoma and CSF resolved.

Conclusion: The 30-day morbidity rate in DBS for secondary dystonia is comparable to that in primary dystonia.

#8896

Long Term Follow-Up in Mohr-Tranebjaerg Syndrome after Pallidal Stimulation

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Keywords: Mohr-Tranebjaerg, DBS, Pallidal stimulation.

Objective: Pallidal deep brain stimulation (DBS) has been established as a treatment option in patients with medically refractory dystonia. Mohr-Tranebjaerg syndrome (MTS) or Dystonia-Deafness-Syndrome is a rare genetic disorder characterized by deafness, dystonia and neurological abnormalities like impaired vision, dementia and cortical blindness. So far little is known about the efficacy of DBS in MTS.

Methods: A 44-year- old man with a history of generalized dystonia, deafness, visual blindness, ataxia and tremor was diagnosed with MTS which was confirmed by genetic analysis. He underwent bilateral stereotactic implantation of DBS electrodes in the posteroventral lateral globus pallidus internus (GPi). Electrode location was confirmed by postoperative stereotactic CT.

Results: Bilateral pallidal stimulation yielded modest improvement of dystonia at 6-months follow-up. During the next four months there was an increase of tremor and ataxia. The initial benefit was lost within the next two years. Extensive reprogramming did not yield additional improvement. After three years of chronic stimulation it was decided to switch off the pacemaker because of loss of efficacy.

Oncology

#8564

Rona Guided Stereotactic Biopsy – Case Report

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Keywords: Ronna, Stereotactic biopsy, Robotic system.

Introduction: Robotic systems have been introduced in stereotactic neurosurgery to meliorate the accuracy in performing surgery, to reduce the operative risk and to improve the diagnostic yield. The project RONNA (Robotic Neuronavigation) includes research and development of innovative and competitive robotic system for use in neurosurgery through the cooperation of public university and the business sector.

Patients and Methods: I.J. (60 y) was admitted to the University Hospital Dubrava due to sudden onset of confusion and weakness of the left limbs. Within neuroradiological imaging we performed contrast enhanced brain MSCT, which showed central necrotic expansive lesion with ring enhancement, surrounding edema, located in the right frontal lobe. The first robot-guided stereotactic biopsy in Croatia was done on the 10 th of March 2016. In local anesthesia using RONNA and commercial neuronavigation system, which served as a confirmation, location of biopsy was defined. We took 4 samples for pathohistological analysis and evacuated 45 ml of liquid cystic content.

Results: There were no operative and postoperative complications. After surgery patient was transferred to the Department, without neurological deficits. Postoperative CT and MRI reveiled

no signs of acute bleeding or ischemia and confirmed that samples were taken from the planned sites. The definitive pathohistological finding confirmed diagnosis of glioblastoma.

Conclusion: In our humble experience robot significantly increases the accuracy and helps the surgeon by giving him additional conformation, all of which increases patients safety. We hope that further clinical use will reduce duration of the surgery and expand the use of robots in neurosurgery.

Pain

#8284

Approaching Foramen Ovale Under Real-Time Fluoroscopy Through Hartel's Entry for Management of Trigeminal Neuralgia: Technical Note

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Keywords: Trigeminal neuralgia, Radiofrquency, Fluoroscopy.

Introduction: Percutaneous cannulation of the foramen ovale to reach the gasserian ganglion has been extensively discussed, starting with Hartel's free hand approach to intraoperative imaging (i.e. by CT or fluoroscopy), stereotaxy and neuronavigation techniques. In this abstract, we will describe a technical note to approach the foramen ovale by real time fluoroscopy using Hartel's entry point to achieve maximal accuracy and efficient radiofrequency lesioning of the Trigeminal ganglion.

Methods: The patient lies supine on a fluoroscopic table with interscapular pad, and moderate head rotation towards the contralateral side of the target thus minimizing the C-arm rotation in both caudo-cranial and lateral direction. This also facilitates the surgeon's position near the head of the patient during the procedure. The Hartel's entry point is then marked with a needle tip. A submental view of the skull is then obtained. The foramen ovale is easily identified by its location at the anterior border of the petrous bone 1–2 cm lateral to its apex. Then locate the foramen medial to the mandibular ramus and lateral to the maxillary air sinus. You need to align the foramen with the metal pointer so you can cannulate the foramen in tunnel view. The needle is then directed towards the superomedial wall of the foramen. Lateral view is then obtained by aligning both auditory meatus together. Then the cannula is slowly advanced to the target trigeminal division. Then, we obtain AP view matching the petrous upper border with the middle of orbital cavity to visualize the trigeminal impression and the relation of the needle to it. Confirm needle location functionally by measuring impedance (usually from 200–400 ohm) and do sensory and motor stimulation at 50 Hz and 2 Hz successively. Finally, do conventional lesioning at 65–70 degree for 60 seconds for 3 cycles and assess pinprick sensation after each cycle to confirm adequate lesioning.

Results: We performed 29 cases from 2013 to 2015 with follow up period ranged from 6 months to 3 years, 27 showed over 75% reduction in VAS score and were classified as excellent response, 4 patient had undergone V1 lesioning, 2 patients of them developed corneal anesthesia with no evidence of keratitis at 1 year follow up. 3 patients had residual area of pain which were managed by repeating the procedure within one week to achieve complete coverage. 2 patients developed motor weakness in mastication, which improved within 6 months, the mean cannulation time was 11.9 min ±6.5, mean threshold painful stimulation was 0.39 V ±0.23, and mean impedance was 288 Ohm >47.

Conclusions: Real time fluoroscopy using Hartel's entry point provides safe and accurate method to locate and approach the trigeminal ganglion in a relatively short time.

#8322

Value of Neuronavigation and O-Arm® in Accurate Intra-Operative Positioning of SPG Microstimulation for Cluster Headache

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Keywords: Neuronavigation, O-arm, Sphenopalatine ganglion, Cluster headache.

Background/Aims: Sphenopalatine ganglion stimulation has been proposed as a novel approach to treat chronic cluster headache. To achieve a therapeutic effect, the surgical lead placement in the pterygopalatine fossa is a crucial step. The present study analyses the role of both neuronavigation and the 3D O-arm® platform in improving the precision of the sphenopalatine ganglion microstimulator implantation.

Methods: Two patients with refractory chronic cluster headache underwent sphenopalatine ganglion microstimulation. Based on a preoperative 3D CT-scan, a neuronavigation system was used to plan the trajectory towards the pterygopalatine fossa. Intraoperatively the microstimulator was implanted using neuronavigation and anatomical landmarks from 2D acquisitions. At the end of surgery a 3D O-arm® data set was acquired to localize the implanted device and to confirm an optimal final position in the pterygopalatine fossa. The O-arm® data set was then analyzed and compared with a postoperative CT image series.

Results: Neuronavigation helped in performing the dissection towards the pterygopalatine fossa, however was not accurate for the implantation of the device. The O-arm® was found to be a precise and reliable control tool providing the same information with respect to the device localization as the CT-scan images obtained postoperatively.

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Conclusion: Neuronavigation has a limited role during the positioning of sphenopalatine ganglion microstimulator but remains useful in the surgical approach to the pterygopalatine fossa. Newer surgical instruments that can be used in correlation with the neuronavigation system should be developed. O-arm® could advantageously replace the postoperative CT to accurately check the position of the microstimulator, without an increase in surgical duration. We hypothesize that the intraoperative use of the O-Arm® could avoid potential second look surgeries for device misplacement.

#8469

Functional Neurosurgery in Trigeminal Neuropathy and Neuralgia. The Force Awakens!

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Keywords: Neuromodulation, Nervus trigeminus, Neuropathy, Neuralgia, Functional neurosurgery.

Introduction: Trigeminal neuralgia and neuropathy are characterized by pain in the face, originating from the trigeminal nerve. The trigeminal neuralgia has a paroxysmal profile and the neuropathy a permanent burning sensation.

The thermocoagulation of the Ganglion Gasseri was the first effective minimal invasive functional neurosurgery therapy in the treatment of trigeminal neuralgia. On the other side the trigeminal neuropathy has always been very difficult to treat with most of the patients having serious problems controlling the symptoms despite elaborate medication. Over the last 8 years the evolution of stimulation protocols (Burst, HD, Whisper, 10 K) as well as the development of new products (IPGs and electrodes) has revolutionized our treatment options especially in the treatment of trigeminal neuropathy.

In our department we are using the complete portfolio of functional neurosurgery to treat these two conditions for more than 35 years now.

Materials and Methods: The aim aof the study is to retrospectively analyse the patients with trigeminal neuralgia and neuropathy we treated from 2007 to 2015 using the complette portfolio of functional neurosurgery.

Results: From 2007 to 2015 we treated 262 patients with trigeminal neuralgia for a sum of 424 Thermocoagulations of the Ganglion Gasseri. 57% were women and 43% men.

In the same period we also treated forty-six patients with a neuropathic facial pain.

The retrospective analysis of the patients with neuralgia showed that:

§ Women with MS had an adequate pain relief for 22 months, men for 16 months.

§ Women and men with recurrent idiopathic neuralgia 16 months.

§ Women with microvascular compression with MVD 41 months, men 46 months.

§ MS patients had a recurrence rate of 48.8%

§ Patients with microvascular compression of the trigeminal nerve had an overall recurrence rate of 32%.

§ Patients with idiopathic neuralgia had a recurrence rate of 24.4%.

The complication rate was under 1.5%, with neuropathy being the main postoperative complication.

The patients with V2 and V3 neuropathy were treated with a PNS System in the Ganglion Gasseri itself. The patients with the V1 and V2 neuropathy were treated with a PNFS System in area of the pain itself. All patients were stimulated with various protocols (Tonic, HD/Whisper, Burst). Both groups of patients showed a reduction of the VAS Score of more than 50%. Both groups achieved a reduction of the pain medication of more than 30%.

Conclusion and Discussion: Trigeminal neuralgia and neuropathy are two sides of the same coin when it comes to treating them. The evolution of neuromodulation products and stimulation protocols add an extra arsenal in the existing options with the ability to adapt the treatment to the patient and achieve definitive control over the symptoms. In conclusion functional neurosurgery, in its full spectrum and portfolio, offers all around treatments with safe, efficient, minimal invasive and long lasting effects.

#8487

Chronic Vagal Nerve Stimulation in Intractable Hiccup. Case Report and Review of Literature

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Keywords: Vagal nerve stimulation – Hiccup – Score evaluation.

Introduction: More than 100 cases for hiccup have been described in literature. In case of intractable hiccup the surgery can improve this disorder. The complete denervation of phrenic nerve seemed to be highly risky so the neuromodulative techniques appear to be justified. We reviev the Literature about Vagal Nerve Stimulation (VNS) in hiccup and add a case report.

Material and Methods: The Literature search found three cases of VNS performed for intractable hiccup. We report a further case of a 68-year-old male presented with continuous, intractable hiccup. His disorder had developed after a partial stomach resection for gastric ulcer performed in 2005 and is characterized by 60 hiccups/minute all day along. After chronic VNS stimulation the hiccup decreased of 50% and the patient improved the sleep. At last follow-up (3 months ago) the benefit is unchanged.

Results: The VNS output current was 2–2.5 Mamph OFF 5' ON 30''. At present only four cases of VNS in intractable hiccup has been reported with complete benefit in two patients and partial benefit in other two at follow-up.

Conclusions: The VNS on persistent hiccup has been reported in few cases after drugs failure administration and no long term benefit from phrenic nerve block. This technique should be standardized in the treatment of intractable hiccups and an uniform score evaluation of the results should be introduced.

#8516

Spinal Cord Stimulation for Ischemic Pain Syndrome (The Siberian Experience)

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Keywords: Spinal cord stimulation, Ishemic pain, Refractory angina pectoris, Peripheral vascular disease.

Aims: Angina pectoris (AP) and peripheral vascular disease (PVD) is a chronic pain conditions caused by coronary and peripheral artery diseases, which can't be relieved by the vascular surgery treatment. Spinal cord stimulation (SCS) is a neuromodulation therapy that appears to be an effective and safe treatment for these patients.

Methods: We had applied SCS in 14 patients with AP and 36 patients with PVD ($n = 50$). The leads were inserted in the epidural space at the Th_1-Th_2 (for AP) and Th_{12}-L_1 (for PVD) levels. Myocardium perfusion scintigraphy (MPS) in AP patients and transcutaneous oximetry (TCO) in PVD patients were performed on admission, on the 7th day and in 1 year after procedure. The visual analogue scale (VAS) was used to assess the degree of pain both in rest and physical activity in all patients.

Results: The patients showed 8.21 ± 0.89 marks according VAS before the procedure and pain relief to 1.78 ± 0.98 marks ($p < 0.01$) after 1 year of procedure in group of AP patients. In group of PVD patients pain impairment was from 9.43 ± 1.25 to 1.03 ± 0.1 marks according VAS. All the patients demonstrated the rise of tolerance to the physical activity. MPS detected the increase in coronary reserve from 9 to 3 prearranged units, TCO showed oxygen saturation's increase from 7 to 70 mm Hg on the shin. There were no any procedural complications.

Conclusions: According to recommendations of Neuromodulation Appropriateness Consensus Committee (NACC) SCS can be recommended as evidence level 2a, degree of recommendation A, for the patients with refractory angina pectoris. And in case of peripheral vascular disease the NACC recommends SCS be utilized prior to the irreversible approach of sympathectomy. Our experience confirmes that SCS is a minimally invasive technique to reduce the pain and improve quality of life with vascular reserve enhancement in AP and PVD patients.

#8531

Microvascular Decompression of Trigeminal Nerve for Chronic Cluster Headache: Report of Two Cases and Brief Review of Literature

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Keywords: Cluster headache, Microvascular decompression, Trigeminal nerve.

Cluster headache (CH) is the commonest of the trigeminal automonic cephalalgias (TAC), it occurs up to 56–400 cases/100.000 habitants and is characterized for repeated attacks of severe, unilateral pain in the orbital, supraorbital or temporal region, lasting 15–180 minutes and occurring from once every other day to 8 times/day. It is associated with one or more autonomic symptoms: conjunctival injection and/or lacrimation, nasal congestion or rhinorrea, eyelid edema, forehead and facial sweating, miosis and/or ptosis, sense of restlessness and agitation. The male/female ratio is reported as 2.5:1. The age of the onset is more frecuently between 32–38 years. The exact cause and pathofhysiology remain unknown, however some neuropeptides in trigeminal innervation have been related (CGRP, substance P and vasoactive intestinal peptide). The attacks are often produced at night time and follow episodic and circadian patterns.

The episodic form of CH affects 85% of cases and up to 10% are affected by the chronic form wich consists on attacks that occur for more than 1 year whithout remission or with remissions lasting less than a month. Only 4% of patients affected by the chronic form of CH are refractary to medical management and therefore suitable for surgical treatment.

The different surgical options include ablative therapies on sphenopalatine ganglion, ablative therapies on V cranial nerve, DBS of the posterior hypothalamus, neuromodulation of occipital nerve, microvascular decompression of sphenopalatine ganglion and microvascular decompression of V cranial nerve, all of them with variable and controversial results.

The microvascular decompression of trigeminal nerve is a non ablative therapie, wich avoids many secondary effects and has been described as an effective surgical treatment. Lovely et al. reported good results with treatment of chronic CH through microvascular decompression of trigeminal nerve, alone or in combination with section and/or microvascular decompression of the intermediate nerve in 28 patients, including 2 with bilateral disease. However, although 22 of 30 procedures (77.3%) resulted in an excellent or good outcome in the immediate postoperative period, the success rate dropped to 46.6% with long-term follow up. Rowed *et al,* Solomon and Apfelbaum, Morgenlander and Wilkins reported similar results.

We describe the experience in our center with 2 cases of microvascular decompression of V cranial nerve for chronic, refractary cluster headache.

#8561

Treatment of Potential Ischemic Pain Syndrome with Spinal Cord Stimulation

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Keywords: Ischemic pain syndrome, Spinal cord stimulation.

Introduction: Analgesics was used to control various pain syndrome for many years. The efficacy of pain control with new innovated pharmacotherapeutics is getting better gradually. However, for ischemic pain, the acceptable outcome of painkillers is not so impressive to free from symptoms. Ischemic pain is not only the unpleasant feeling, but it will progress to tissue damage on involved limb. As early stage of ischemic limb, patients, usually, presented simply painful without skin lesion or vascular occlusion in imaging study. These symptoms will be confused to differentiate pain origin between lumbar root impingement and insufficient microcirculation on involved limb.

Method and Material: In past 10 years, 420 cases failed back surgery syndrome were surveyed with plain dynamic X-ray, MRI and electrophysiologic studies to verify pain origin. One hundred and thirty-four cases (32%) were no nerve impingement or instability on spine even presented significant lower limb pain. In these cases, painful area focuses on lower limb rather than on lumbar spine. Neither skin lesion nor vascular compromising was found on involved limb.

Stress myocardial Thallium-201 scintigraphy were instructed with supine position after an exercise SPECT imaging. The result showed an insufficient microcirculation of muscle at involved limb. The average pain score VAS is 7.11.

Of 134 cases, 62 patients received spinal cord stimulation (SCS) treatment. Stimulator (Medtronic co.) were implanted at epidural space around T10-T11. Other patients prescribed with analgesics, physical therapy or hyperbaric oxygenation due to economic reason.

Results: All cases were evaluated on OPD follow-up regularly. After 12 months of treatment, VAS in the group of SCS treatment improved with 7.27 vs. 3.43, compared to the other group with 7.18 vs. 6.84. The walking distance increased by an average 3.7-fold in SCS group. Fontaine stage and sleeping quality also had significant improvement.

Conclusion: Spinal cord stimulation was used to treat the intractable pain for many years. The majority of candidates were emphasized on neuropathic pain. In recent decays, many analgesics were developed for pain reduction instead of spinal cord stimulation. Nevertheless, the effect of pain control of ischemic limb is still limited. For those patients with atypical neuropathic pain, muscle perfusion scanning might be a possible way to find out the early stage of PAOD. Using the spinal cord stimulation to treat ischemic limb is not only pain disruption but also refill the microcirculation in hypoperfused tissue.

#8600

Dorsal Ganglion Stimulation with Novel Minature Lead Wireless Stimulator

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Keywords: DRG stimulation, Wireless stimulator, Complex regional pain syndrome, Failed-back surgery syndrome.

Introduction: DRG stimulation is a modern and effective neuromodulative method of treatment of chronic neuropathic pain with dermatomal distribution. The Freedom Stimulator is the smallest implanted stimulator system. Freedom stimulator (Stimwave, CA, USA) is implanted through a needle.

Aim of the study was to assess the efficacy and usefulness of this system in our department.

Material: We evaluated the effects and sustainability of the analgesic effects of this type of stimulation in 3 patients with chronic neuropathic pain of foot in two cases and in thigh in one case. Diagnoses were following: CRPS t.II in foot pain caused by cauda equine injury, idiopathic neuropathic peripheral pain located in foot and FBSS with distribution in right thigh.

Methods: In two patients electrode and stimulator leads were implanted into the intervertebral foramen of L5/S1 in two cases and L3/L4 in one case. Stimulator were charged with the use of the wearable antenna externally worn by patients.

Results: In 3 patients after one month of stimulation we observed significant reduction of pain assessed in VAS score: 90% reduction of intensity of idiopathic neuropathic pain, 60% reduction of CRPS t.2 and 70% reduction in FBSS.

Conclusions: Stimulating system seems to be effective, minimally invasive and convenient for patients.

#8604

Potential Psychological Predictors of Motor Cortex Stimulation Efficacy for the Treatment of Chronic Neurogenic Pain Syndromes

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Keywords: Motor cortex stimulation, Chronic pain, Neurogenic, Psychological, Predictors.

Background and Objectives: Chronic electrical motor cortex stimulation (MCS) is the youngest among the neuromodulation methods for the treatment of chronic neurogenic pain syndromes. Currently, the most common indications for MCS are central post-stroke pain, atypical facial pain, phantom pain. There are

some contraindications: the lack of effect of rhythmic transcranial magnetic stimulation (rTMS), clinically significant mental disorders, cognitive disorders disallowing the patient to learn the skills of treatment with the stimulation system, severe somatic diseases. Despite relatively well-defined indications and patient selection criteria adequate analgesia in long-term follow-up cannot be achieved, even in the absence of technical and iatrogenic complications. In this regard, the question about the predictors of MCS efficacy is not still closed. Our study is aimed to evaluate potential psychological prognostic for MCS efficacy for the treatment of neurogenic pain.

Materials and Methods: The study includes patients with chronic neurogenic pain syndromes, long taking medication with lack of efficacy, having indications for MCS implantation. To date, we have retrospectively included and analyzed 11 patients (6 men and 5 women), who was treated in N.N. Burdenko Neurosurgery Institute between 2005 and 2010. The approximate age of the patients was 53 y.o. Two patients (1 male and 1 female) suffer from right-side trigeminal neuralgia, occurred due to multiple sclerosis. In two male patients there is a phantom pain of post-traumatic genesis. Two male and one female patients suffer from post-stroke central pain syndrome in one half of the body. In 3 patients (1 male and two female) have a complex regional pain syndrome, occurred after the injury of the right brachial plexus. One patient developed pain in his left hand after the removal of intradural extra medullary tumors of the spinal cord at the cervical level, subsequent DREZ-lesion was not effective. Before surgery all the patients had been neurologically examined and tested with following scales: 36-Item Short Form Survey (SF-36), Spielberger's personal and situational anxiety, Beck's depression questionnaire, The Pain Catastrophizing Scale and Chronic Pain Coping Inventory (CPCI). All patients have been being examined in 1-year or more follow-up after MCS implantation and then divided into 2 groups of treatment efficacy. The effectiveness criterion was 30% and more pain relief according to the visual analog scale (VAS).

Results: Pain relief due to MCS was more than 30% in 7 patients. In 4 patients pain relief was below 30%. The main quality of life parameters, namely General Health (GH), Vitality (VT), Social Functioning (SF) and Mental Health (MH) was higher in the group of high MCS efficiency, while Role-Emotional parameter was higher in low MCS efficiency group. There were no differences in other quality of life parameters between the groups. Levels of depression and reactive anxiety did not differ between the groups. Personal anxiety was higher in the group of low MCS efficiency. Expression of wellness-focused coping strategies (Coping Self-Statements, Task Persistence) and the strategy of Seeking Social Support was higher in the group of high effective MSC as compared with group of low effective MCS. Pain catastrophizing levels was higher in the group of high effective MSC.

Discussion: We can suggest, that personality and psychological characteristics of patients (such as chronic pain coping strategies, personal anxiety, pain catastrophizing) may influence on the efficacy of MCS for the treatment of chronic neurogenic pain syndromes. Furthermore, MCS can be assumed to affect the basic quality of life parameters. Further follow-up observation and further studies are necessary to determine predictors of MCS efficacy.

#8615

Microvascular Decompression for Trigeminal Neuralgia – A 102 Patients Surgical Series from Centro Hospitalar e Universitário de Coimbra

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Keywords: Trigeminal neuralgia, Microvascular decompression.

Introduction: Trigeminal neuralgia (TN) is reportedly one of the most excruciating orofacial pain syndromes. In most cases, the cause is idiopathic. The goal of microvascular decompression (MVD) is to decompress the trigeminal root from offending vessels, aiming at a permanent cure with no or little sensory deficit.

Methods: 102 patients submitted to MVD to treat trigeminal were selected, retrospectively, from the data of the Neurosurgery department in Centro Hospitalar e Universitário de Coimbra.

A telephone questionnaire was performed to inquire patients about their experiences after surgery.

Outcome was evaluated by the Barrow Neurological Institute scale.

SPSS was used for statistical treatment and statistical significance was considered as a p-value <0.05.

Results: A total of 102 patients were enrolled, with a mean age of 61.68 at time of surgery. 55.9% were women, and 44.1% were men.

95% of the cases had a typical presentation, with a right side involvement in 60.8%. V2-V3 was the pain territory most often encountered, representing 33.3% of the cases, followed by V1-V2 territory (24.5%) and V2 (19.6%). 89.7% had some kind of vascular compression, confirmed at surgery, 69.1% of which was of arterial nature. AICA was the most frequently involved artery, in 53% of the cases. Gore Tex was the more often used prosthesis, in 79%, followed by Teflon in 18%, Dacron in 2% and Silastic in 1%.

There was a 17.7% complication rate, with hipostesia of one of the V pair branches being the most frequent one (47.6%).

Symptomatic relief was achieved in 91%, with total pain relief in 67%. Only 4% continued with uncontrolled pain after surgery. 27% had recurrence of symptoms.

There was a significant statistical difference ($p = 0.005$, Pearson Qui-Square) in the outcome between the different kind of vessels involved. In fact, severe uncontrollable pain was associated with compression by the ACS artery and better results were noticed in cases with compression by the AICA artery.

The type of prosthetic material used, influenced the clinical recurrence ($p = 0.016$, Pearson Qui-Square), and patients with Gore-Tex prosthetics had a larger recurrence rate. There was also a significant statistical difference between the type of prosthetics and the complication rate ($p = 0.022$, Pearson Qui-Square), Gore Tex being implicated in more cases of complications.

The territory of involvement had influence in the kind of complication associated (p-value 0.032, Pearson- Qui Square).

Conclusion: MVD is a safe and effective procedure to relieve typical TN and our series demonstrated good surgical results, similar to other series in the literature.

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Preoperative identification of neurovascular compression, surgical planning and choice of prosthetic material have important implications in the clinical outcome.

#8626

Microvascular Decompression or Neuromodulation in Patients with SUNCT and Trigeminal Neurovascular Conflict?

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Keywords: Neuromodulation, Microvascular decompression (MVD), Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT).

Objectives: To assess the relative effectiveness of neuromodulation and trigeminal microvascular decompression (MVD) in patients with medically intractable short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT).

Methods: We present two patients with medically refractory SUNCT who underwent MVD following beneficial but incomplete response to neuromodulation. One of them had occipital nerve stimulator and the other had deep brain stimulator. Brain MRI was performed and confirmed neurovascular conflict with the ipsilateral trigeminal nerve in both patients.

Results: Although neuromodulation provided significant benefit in both patients, it did not deliver complete relief from pain and management required numerous postoperative visits with adjustment of medication and stimulation parameters. Conversely, MVD was successful in eliminating symptoms of SUNCT in both patients with no need for further medical treatment or neuromodulation.

Conclusion: Surgical treatment of medically intractable SUNCT is challenging because of the severity and rarity of the condition combined with the paucity of reports in the literature. Over the last decade, peripheral and central neuromodulation as well as trigeminal microvascular decompression have emerged as efficacious treatments. The aim of this report is to highlight that microvascular decompression may be preferable to neuromodulation in the subset of SUNCT patients with ipsilateral neurovascular conflict. Neuromodulation should probably be reserved for those patients without conflict or for those who fail to respond to MVD.

#8834

Severe Pain and Oedema Due to a Widespread Lymphangioma: Disappearance of Symptoms and Reduction of Lesion with Spinal Cord Stimulation

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Keywords: SCS, Lymphangioma, Chronic pain syndrome.

Background: The efficacy of epidural spinal cord stimulation on chronic neuropathic pain due to failed back surgery syndrome or nerve root lesions is well reported. There is even literature reporting the effects of spinal cord stimulation in controlling peripheral vascular lesions as in peripheral arteriopathies or diabetic neuropathies and in Complex Regional Pain Syndrome type II. This is probably due to an effect of epidural spinal cord stimulation mainly on the parasympathetic nervous system.

Case Description: A 14 years old boy affected, since birth, by a quickly growing widespread lymphangioma at the pelvis and right thigh, was submitted to repetitive surgical procedures to try to reduce its extension. Recurrence always occurred. Due to a massive swelling of his right lower limb and a wide painful area all over the pelvis and right lower limb, the patient lately lost his autonomy being almost bedridden or wheelchaired. On January 2015 the patient was submitted to the implant of a low dorsal epidural eight leads MR compatible electrode connected to an MR compatible stimulator. The patient, one month after the implant, completely recovered his autonomy with a marked shrinkage of his right lower limb and nearly disappearance of pain. He returned to a normal daily activity. A hip-MR showed partial reduction of the lesion, one year later. The patient is still nearly free from pain.

Conclusion: This is the first case report of severe chronic pain syndrome due to a widespread lymphangioma successfully treated by means of epidural spinal cord stimulation.

Psychiatric Disorders

#8392

Basal Ganglia Disinhibition in Tourette Syndrome; Patient and Animal Model of Tic Expression

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Keywords: Tourette syndrome, Deep brain stimulation, Tic, Globus pallidus, Neurophysiology.

Introduction: Tourette Syndrome (TS) is thought to result from malfunctions in the cortico-basal ganglia (CBG) pathway. The striatum controls the output of the basal ganglia (BG) through two pathways: the direct pathway to the globus pallidus internus (GPi) and the indirect pathway to the GPi through the globus pallidus externus (GPe). Functional and animal models of the BG provide two models with potential mechanisms for hyper-behavioral disorders like TS. First, hyperkinetic symptoms may originate from abnormal focal activation of striatal neurons which inhibit the activity of a sub-population of GPi neurons, leading to a phasic disinhibition of their targets. Second, striatal disinhibition may lead to reduced tonic inhibition exerted by the GPi on its thalamo-cortical targets. Both theories suggest that this leads to a transient action expression, such as a tic. The emergence of deep brain stimulation (DBS) targeting the GPi in TS provides an opportunity to directly observe the neuronal activity in the BG.

Methods: We analyzed the neuronal activity in both the GPe and the GPi of seven awake TS patients (TSP) who underwent physiologic mapping for placement of bilateral DBS electrodes in the anterior GPi. Up to 5 microelectrodes were used to record the neuronal activity along the trajectory. Recording took place from 10 mm above target to 4 mm beneath target in 0.5–1.0 mm steps. Moreover, we evaluated possible similarities and differences with the neuronal activity recorded from the Non-Human Primate (NHP). We observed normal Non-Human Primates (NP) and the motor tic NHPs model (TMP) after implanting 2 chambers stereotaxically to allow bilateral access to the motor cortex and the BG. The tic model was observed following microinjections of $GABA_A$ antagonist (bicuculline) into the motor region of the striatum. The animal's behavior was continuously monitored by video cameras and EMG recordings and multiple microelectrodes were used to simultaneously record neuronal activity from the GPe and GPi.

Results: A total of 199 single neurons were recorded from seven awake TSP and they were identified as GPe (n = 64) or GPi (n = 135) neurons based on their location and trajectory history, including border cells and reduced background activity. The mean firing rates were 48.25 ± 3.8 spikes/s and 47.17 ± 2.8 spikes/s for GPe and GPi, respectively. We compared these firing rates to the firing rates of neurons that were recorded from the NP and the TMP. A total of 136 neurons (72 GPe, 64 GPi) were recorded from two NPs, and 151 neurons (73 GPe, 78 GPi) were recorded from three TMPs.

A significant decrease was found in the baseline firing rate of both the GPe and GPi neurons during the tic state (both TSP and TMP), compared with the NP (two-sample t-test, $p < 0.01$). For TSP, the firing rates positively skewed (0.99 and 1.06 for GPe and GPi, respectively) by a minority of high firing rate neurons. These results were in contrast to the distributions of the NHPs' neurons (NP: 0.08 and 0.25; TMP: 0.48 and 0.11, for GPe and GPi respectively). The skewness indicates that the firing rate of most TSP neurons is even lower, with a subpopulation of high frequency discharge neurons. While the firing rates were similar between GPe and GPi neurons, the firing patterns of the neurons in each nuclei were different. Both the coefficient of variation (CV) and the Fano factor (FF) were higher in GPe neurons, in line with their typical pauses, compared to GPi neurons. In the GPi, the CV and the FF were significantly higher during tics, in comparison to the normal state, reflecting increased bursting.

Conclusion: The combination of data from human patients and the NHP model of the disorder provides novel insights into the release of abnormal actions by the CBG pathway. Reduced baseline firing rate was found in both segments of the globus pallidus of the TSPs and the TMPs compared to the NPs. The two striatal cell populations contributing to the direct and indirect pathways of the BG are disinhibited and provide increased inhibition to both the GPe and GPi. This results in a tonic reduced inhibition on thalamic and cortical regions which is phasically modulated around the tic time.

#8462

Deep Brain Stimulation in Bed Nucleus of Stria Terminalis and Medial Forebrain Bundle in a Patient with Major Depressive Disorder and Anorexia Nervosa

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Keywords: Deep brain stimulation, Depression, Anorexia nervosa.

Introduction: In deep brain stimulation (DBS), thin quadripolar electrodes connected to a neuropacemaker are implanted into subcortical central structures of the brain where pathological neuronal activity is modulated with electrical current. The method has revolutionized the treatment of Parkinson's disease and other movement disorders and is under investigation for, among others, some psychiatric conditions.

DBS has in this group shown some promising results, but the material is limited and heterogeneous, consisting mainly of small

non-randomized studies with electrodes implanted in many different brain target structures (1).

Here we present a patient with severe major depressive disorder (MDD) and co-morbid anorexia nervosa treated with DBS in the medial forebrain bundle (MFB) and subsequently in the bed nucleus of stria terminalis (BNST).

Case Presentation:

History: The patient, a 60-year woman, had childhood onset of anxiety and anorexia nervosa, with symptoms of anxiety connected to food intake, restricted eating and later on purging. The course of the eating order was remitting and relapsing with episodes at age 14, 28 and most recently at age 44. The last episode had a prolonged course and over time her depressive symptoms became more and more severe and since the age of 47 her main problem was MDD, with significant symptoms of anxiety. By the end her eating disorder had clear depressive components with thoughts of being a burden to relatives, not being worth to eat and suicidal ideations about starving to death. At the age of 54 the patient was committed to a closed psychiatric ward.

Treatment: The patient had tried and failed psychotherapy, several different SSRI, SNRI, NaSSA, MAOIs, tricyclic antidepressants, mood stabilizers, neuroleptics and ketamine infusions, with little or no effect. The only treatment providing relief was ECT, and the patients had received since many years three sessions of ECT every fourth week. Unfortunately ECT resulted in a gradual loss of memory, finally removing most of her memories from before her 30 years of age. Attempts to reduce the frequency of ECT sessions failed since this resulted in several suicide attempts while being admitted.

Therefore after extensive screening and informed consent, the patient was included in an ongoing study of DBS for MDD. The MFB was chosen as target based on a recent report, which highlighted the acute and quick effect of this treatment (2).

When evaluated before surgery at baseline the patient weighted 40 kg with a body mass index (BMI) of 16.6. She was deemed severely depressed. She scored 43 points on MADRS, 22 on HAM-D and 34 on HAM-A. She preferred lying alone in a dark room. She exhibited reduced facial mimic. She responded adequately to questions, but with short sentences and a monotonous voice.

At age 56, the patient underwent implantation of two DBS electrodes (Medtronic model 3389) in the MFB in the posteromedial hypothalamic area just anterior of the red nucleus. Stimulation was initiated two days after surgery. When the patient returned one week later the effect was perceived as dramatic. The patient considered herself to be 'quite happy'. She had a normal facial mimic, spoke fluently and smiled occasionally.

Bipolar stimulation was delivered using three contacts on each side, at 130 Hz, and 60 uS. The voltage was gradually increased and after 4 months was 2.8 V on the left side and 3.0 V on the right. Further increase was not possible since it caused blurred vision. At 6 months MADRS was reduced to 26 points, HAM-D 22 and HAM-A 21.

Ten months after the procedure the patient complained of blurred vision. Numerous adjustments of stimulation and cessation of lamotrigin (due to possibility of the drug to attenuate visual side-effects) were tried in the following period without success. The symptom was partly stimulation induced, but even after the stimulation had been turned off for 2 weeks, some minor symptoms remained. The stimulation was restarted with a voltage reduced to a level where the side effects were tolerable, however, with a reduced effect on her psychiatric symptoms.

Two years after the first procedure the patient was therefore re-operated, with implantation of bilateral electrodes (Medtronic model 3387) in the BNST. The patient received monopolar stimulation through two contacts on each electrode and gradually increasing voltage. At 12 month the patient had 130 Hz, 120 uS and 4.3 V bilaterally. The stimulation in the MFB was simultaneously reduced and turned off without any signs of deterioration.

Outcome and Follow-Up: The improvement seen after BNST DBS was more gradual but very profound. Nine months after surgery the patient was released from the psychiatric ward and returned to her home. Prior to this she had been subject to hospital care, initially due to her eating disorder and lastly due to severe MDD with suicidal ideation, for almost 4 years. She is now living fulltime at home with her family and participating in social gatherings and outdoor activities. She considers herself to be profoundly improved and at 12 months her MADRS was reduced to 13 points, HAM-D scored 6 and HAM-A 5 points.

During the whole postoperative periods, neither of the surgical procedures had any significant effect on her anorexia, in terms of BMI. However, following the second procedure all her anxiety for food and eating vanished. She has virtually stopped vomiting, her food intake is more stable and less prone to large variations, and tube feeding could be cessated. However, in the words of the patient, she continues out of habit to eat just enough to keep her weight stable, even in the absence of anxiety or obsessive thoughts. However, she is now motivated to start behavioral training to change this pattern.

Discussion: According to WHO, depression is the most common cause of disability with a prevalence of 3–5%(3), and the STAR*D studies have demonstrated the limitations of conventional treatments (4). Not only is depression associated with a suffering for the patients, an often severe social handicap and a reduced quality of life, but also with a significant mortality. It is estimated that 90% of the suicides are related to psychiatric diseases, the most common cause being depression, where the mortality due to suicide is around 10–15% (5).

Anorexia nervosa has one of the highest mortality rates of any psychiatric disorder and the presence of anxiety and mood disturbances portends a worse prognosis of the disorder (6). As for depression conventional treatment methods have demonstrated limitations. Pharmacological methods have been shown to be ineffective in anorexia nervosa (7). Even with psychotherapy and self-help programs, where effectiveness ranges from 60–70%, there remains a group of patients with intractable symptoms (8).

Even though the majority of patients will respond well to non-interventional therapy, there remains a significant group in both depression and anorexia nervosa, in whom conventional treatment will yield little or no relief of symptoms. In severely affected patients where therapy resistant symptoms have caused a high degree of suffering and handicap, interventional procedures in the form of stereotactic functional neurosurgery might be indicated. The experience of these experimental procedures remains, however, still limited.

A total of 100 patients treated with DBS for MDD in nine different studies and several brain targets have been published {Naesstrom, 2016 #141} (9). The most common targets are the subcallosal cingulate gyrus (SCCG)[9], the nucleus accumbens (NA) and the ventral caudate/ventral striatum (VC/VS)(10–12).

The inferior thalamic peduncle and the lateral habenula were the target in two case reports (13, 14). The most recently published brain target for DBS in depression is the MFB, where results have been presented for seven patients (2). The results of DBS for depression have been generally promising, although recent blinded randomized multicenter studies in the US have failed to show benefit from active stimulation compared to sham stimulation (11). Concerning the BNST this target has only been published in one study of DBS for obsessive compulsive disorder (OCD), but not for MDD (15).

In our patient the MFB, connecting the amygdala, ventral tegmental area, NA, ventromedial and lateral nuclei of the hypothalamus, was initially chosen as target since the onset of effect has been reported to be rapid (2). A fast onset of effect was deemed essential considering the patients dependency on ECT and the fact that ECT may not be possible to do after DBS implantation. Blurred vision following this procedure has been described in the original publication (2), even though not in the way described here with late appearance and semi-reversibility.

When a second surgery was considered indicated the BNST, a part of the anxiety-regulating network between amygdala, hypothalamus, thalamus and orbitofrontal cortex (15), was chosen as target. This decision was based on our own experience of the effect of BNST DBS for concomitant depressive symptoms and anxiety in patients with OCD and generalized anxiety disorder (GAD) (unpublished data). Furthermore, studies have pointed out BNST as an important brain structure involved in anorexia nervosa and anxiety disorders (15–18).

Even though the indication for this procedure was MDD, it would not have been unreasonable to expect a positive effect on the patient's concomitant anorexia. Effects of improved mood and anxiety could potentially disrupt important illness-maintaining factors. The improvement of this patients mood, anxiety and quality of life, even with remaining sign of underweight, is promising, in view of the well known poor response of underweight patients to conventional pharmacological and psychological therapies. In the literature DBS for anorexia has been performed on three different brain targets in 14 patients, several with concomitant MDD, OCD or GAD, published in five reports. The SCCG was targeted in seven patients (19, 20), NA in six (21, 22) and the VC/VS in one (23). Most patients in this heterogenous material seem to have benefited to various extents from the procedures.

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#8463

Deep Brain Stimulation for Obsessive-Compulsive Disorder. Knowledge and Concerns among Psychiatrists, Psychotherapists and Patients

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Keywords: Deep brain stimulation, Obsessive-compulsive disorder, Concerns.

Introduction: Obsessive-compulsive disorder (OCD) is a chronic disorder affecting approximately 2% of the population. It is characterized by persistent obsessive, intrusive thoughts generating anxiety, and related compulsions (tasks or 'rituals') with the function of neutralizing the distress [1]. This disorder is one of the most disabling psychiatric disorders and it comes with a significant mortality. Alonso *et al* suggest that 10–27% of the patients might attempt suicide during their lifetime [2]. Further, up to 10% of patients with OCD continues to demonstrate severe therapy-refractory symptoms despite trying multiple available treatments [3 4]. New treatments are currently under evaluation, including deep brain stimulation (DBS), which modulates brain circuits hypothesized to be implicated in OCD. DBS is an established treatment for severe therapy-refractory Parkinson's disease, dystonia and essential tremor [5] and is currently evaluated for a number psychiatric disorders. The most well studied of these psychiatric disorders is OCD, where data from more than 100 patients with severe OCD has been published. The majority of patients were evaluated within a large number of mostly small and non-randomized studies targeting different brain structures. However, the results have been promising with a symptom reduction typically about 50% and minor side effects [6]. DBS for OCD is not an established therapy, but has received an FDA approval as a 'humanitarian device exemption'[8], thus advancing further forward from experimental to clinical use.

DBS trials for psychiatric conditions require collaboration between multidisciplinary teams highly specialized in DBS, participating patients, primary psychiatric health care providers and often also involvement of other caretakers and family members. This invasive and (probably) life-long treatment, differs considerably from the established therapies, and was in one study ranked as the least preferred novel treatment among inpatients with OCD [7]. It is therefore of importance to get an understanding of the level of knowledge and existing concerns among both medical staff and patients regarding this novel therapy. Such data can be of value to both the professional and public debate, guidelines and policymaking concerning DBS for OCD.

A few publications have been presented regarding quality of life and experiences in OCD patients after treatment with DBS [9, 10]. The authors are, however, unaware of any studies that have examined the knowledge and attitude of DBS in patients with OCD not enrolled in a DBS study. The same is also true regarding their medical mental-health care contacts; psychiatrists and psychotherapists. Therefore, the aim of this study was to identify level of knowledge and concerns, which might be relevant for future study designs and creation of information targeting healthcare professionals and patients.

The study was conducted through a web-based survey, specifically aimed to psychiatrist, cognitive behavioral therapy (CBT) psychotherapists and patients with OCD. Given the relatively small sample sizes, and the paucity of previous research in this area, the study was exploratory.

Materials and Method: Three web-based surveys were constructed for psychiatrist, patients with OCD and therapists with experience of CBT, respectively. The surveys contained questions regarding age, sex, previous knowledge of DBS, source of knowledge, attitudes and concerns towards the therapy. The patient survey included additional questions regarding self-assessed severity of the disorder and current treatment regime. The link to the web-survey was distributed among psychiatrist in the northern region of Sweden and a national CBT psychotherapist group. For patients with OCD, a link was published at the website of the national Swedish OCD patient-support group. The data was analyzed using the statistical tool SPSS, version 22. The project was approved by the Umeå University board of ethics.

Results: A total of 65 patients with OCD, 44 psychiatrists and 52 psychotherapists responded to the survey.

Patients: In response to the question how large an impairment OCD had on their social and professional life 3.1% answered no, 15.4% minor, 24.6% moderate, 41.5% major and 15.4% extreme impairment. Of the patients 38.5% had a combination of pharmacological therapy and psychotherapy, 35.4% only pharmacological therapy and 7.7% only psychotherapy, while 18.5% received no current treatment. 29.2% had knowledge of DBS for OCD prior to the survey. A majority; 94.7% listed media, such as internet or newspapers, as source for the information. Additionally, 15.7% had also received information about DBS from their physician and 10.5% from patient-support groups. 58.5% of the patients were positive to consider undergoing DBS for OCD. Males were more positive than females (p-value 0.05), but no differences were seen regarding age. A possible trend could suggest that patients with prior knowledge of DBS were more positive (p-value 0.167). The most common concerns regarding DBS were; adverse-effects of stimulation (61.5%), possibility of lack of effect on OCD symptoms (60%), change in personality (56.9%) and complications of anesthesia or surgery (56.9%). No significant correlation was seen between these four concerns.

Psychiatrists: Of the responders 57% were certified psychiatrists and 43% under specialist-training in psychiatry. 93.2% had knowledge of DBS for OCD prior to the survey. A majority: 78% listed scientific sources, such as research journals, as source of information. Additionally, 58.5% had also received information about DBS from colleagues, 14.6% from media and 9.7% from patients. After being presented with a list of inclusion and exclusion criteria for DBS for OCD 50% estimated that their clinic had 2–5 patients that could fulfill these criteria, 34% 6–10 patients, 14% >10 patients and 2% no patients. 95% were positive to refer patients for DBS for OCD. The most common concerns regarding DBS were; resistance from patients to undergo neurosurgical treatment (63.6%), complications of surgery or anesthesia (54.5%), difficulty to identify eligible patients (52.3%) and ethical concerns with neurosurgery (29.5%).

CBT Psychotherapists: All responders had experiences with CBT for OCD, 46% had a degree in psychology and the re-

mainder had additional training in CBT. 40.4% had knowledge of DBS for OCD prior to the survey. A majority; 61.9% listed scientific sources as source of information. Additionally, 57.1% had also received information about DBS from colleagues, 28.5% from media and 3.8% from patients. After being presented with a list of inclusion and exclusion criteria for DBS in OCD 54% estimated that their clinic had no patients that could fulfill these criteria, 38% 2–5 patients, 4% 6–10 patients and 4% >10 patients. 94% were positive to DBS for OCD. The most common concerns regarding DBS were; complications of surgery or anesthesia (63.5%), change in personality (38.5%), ethical concerns with neurosurgery (34.6%) and possibility of lack of effect on symptoms (34.6%).

Discussion: Of the OCD patients 29% had knowledge of DBS prior to the survey. The majority had obtained this information through media and there was a non-significant trend suggesting that patients with previous knowledge of DBS were more positive to undergoing such treatment.

It has previously been pointed out that patients educate themselves and build their hopes from uncritical media sources [14, 15], which might be a problem since media cover on DBS tend be overly optimistic with minimal coverage of risks. Concern has also been raised for DBS gaining public popularity before a full evaluation of effectiveness and adverse-effects in psychiatric indications is undertaken [11–13].

This highlights the importance of establishing a dialogue between experts and the general public to foster a better understanding of the possibilities and limitations of DBS. Ultimately, scientists and physicians in the field need to consider the public portrayal of DBS for OCD, to ensure realistic hopes.

In comparison the main source of information for psychiatrists and psychotherapists consisted scientific sources and colleagues. The waste majority of psychiatrists (93.1%) and almost half of the CBT therapists (40.3%) had previous knowledge of DBS. This could reflects the high interest for the field, which can be seen in the increasing number of publications related to DBS for psychiatric indications [16].

Considering the novelty and invasiveness of DBS in psychiatry, an unexpected majority of psychiatrists (95%), CBT psychotherapists (94%) and OCD patients (58.5%) were positive to DBS as a therapy for OCD. However, there is a risk for selection bias with primarily individuals with an interest in DBS participating in the study. That over half of the patients could consider treatment with DBS contrasts with a previous study from 2010 by Patel et al., where DBS was ranked as the least preferred investigational treatment among patients with OCD [7]. Similarly with Patel et al. we found that males were more positive towards DBS than females.

The positive attitude towards DBS among psychiatrists and CBT psychotherapists is reassuring considering the potential need for medical follow up for future DBS OCD patients in their own community. Two commonly mentioned concerns among psychiatrist were resistance to neurosurgery among potential patients and the difficulty to identify eligible candidates. This could represent a lack of knowledge of selection criteria for OCD trials and risks and possibilities of DBS. Strategies to communicate selection criteria for patient referral to psychiatrist and develop clear psychiatric postsurgical follow-up strategies for the patients' primary psychiatric contacts will be needed in the future. It will further be of importance to optimize care and transfer of knowledge to local psychiatric health contacts for this novel patient group. Furthermore, CBT has been suggested as a promising augmentation of DBS in OCD [10 17]. This encourages an increased involvement of CBT psychotherapists.

Complications from surgery and anesthesia was a common concern in all three groups. This is similar to Leykin et al, where participants in a DBS-trial for treatment-resistant depression correctly identified the surgery itself as the riskiest part of the study [18]. As pointed out by Lipsman et al. 'Although DBS is minimally invasive neurosurgery, it is the maximally invasive psychiatric treatment available' [19]. DBS in psychiatric disorders have the advantage of being able to build on 20 years of experience with DBS in movement disorders. The surgical procedure and the risk for complications does not differ greatly from its use in more well studied indications e.g. Parkinson's disease [20].

Side-effects of the stimulation was a main concern in the patient group. Compared to the extensive data on surgical complications, there is limited knowledge about the potential stimulation related adverse effects of DBS in psychiatric disorders. Multiple different anatomical targets are under evaluation in OCD (nucleus accumbens, ventral capsule/ventral striatum, subthalamic nucleus, internal capsule, inferior thalamic peduncle, bed nucleus of stria terminalis) and they differ in probability and quality of stimulation induced side-effects [6]. Related to the issue with multiple targets under investigation is the concern from patients and CBT psychotherapists of the possibility of limited effect of DBS on symptoms. Thus, further research is needed to establish efficacy and safety of the different targets for OCD.

The use of DBS in OCD and psychiatric disorders faces a number of unique ethical challenges. It might therefore not be surprising that ethical issues with psychiatric neurosurgery were one of the main concerns among the psychiatrists. Hence, it is reassuring that the topic is often discussed in the literature [12 21–25].

The possibility of DBS induced personality changes was the second most common concern among CBT psychotherapists and the third in the patient group. The concept of personality is a complex question and it is not possible from this survey to know what the groups would define as a change. However, the possibility of stimulation induced changes in personality is currently one of the most discussed clinical side effect and ethical concern for DBS in psychiatric indications [21 26 27]. Most of the authors suggest that positive changes of important elements of personality, such as mood and cognitive behavior, should rather be an intended outcome rather than an unwanted, coincidental side-effect. There are few reports of perceived positive and negative changes in personality after treatment with DBS in patients with Parkinson's disease [28 29]. Concerning OCD a small study by Gabriels et al. found no adverse changes in personality when using self-rated personality inventory in three patients treated with DBS in the internal capsule [30]. However, empirical studies systematically looking at the effects of DBS on personality in psychiatric patients are still missing.

Considering eligibility of patients, over half of the psychotherapist reported that they had no OCD patients that would fulfill the presented inclusion criteria for DBS. This was in contrast to the psychiatrists, where only 2% estimated that they had no patients fulfilling the inclusion criteria. This discrepancy could be due to psychotherapists encountering patients motivated and eligible for CBT therapy, hence with a less severe form of the disorder, while psychiatrists might encounter a greater diversity of OCD patients, including some with severe symptoms. A study using data from a

naturalistic clinical sample found that meeting the stringent criteria to qualify for DBS is rare among the general OCD population [31]. The question of the potential need for DBS in OCD and how to determine the candidates that will most likely benefit from the therapy has still to be determined.

Conclusion: The interest and research for DBS in psychiatric disorders have surged the past decade since the first publication of Nuttin et al. 2003 and the therapy is hoped to have the potential to relief symptoms in some of the most disabling disorders known to humankind [32]. With the FDA approval for a 'humanitarian device exemption' and the increasing number of worldwide implantations, DBS for OCD is already moving from experimental to clinical use [6 8]. Thus increasing the number of potential patients that will be in need of ongoing follow-up care by professionals in mental health care. This underlines the importance of proper education and information for potential DBS patients and their healthcare contacts. The current knowledge and experience of DBS in OCD mainly derives from small non-randomized studies. There are still plenty of challenges identified by the participants of this study: source and quality of information, efficacy, potential adverse effects and eligibility. For all of those, the current evidence base is very limited; therefore, a broad research agenda is needed for studies going forward.

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#8556

Bilateral Anterior Cingulotomy for Chronic, Treatment-Refractory Depression: Effects on Interpersonal Functioning and Relationship to Symptom Change

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Keywords: Anterior cingulotomy, Treatment-refractory depression, Social functioning.

Background: Interpersonal dysfunction has long been recognised as a core component of depressive illness. Some studies suggest that interpersonal difficulties may be persistent and recover more slowly than symptoms. Difficulties in interpersonal functioning may also reflect ongoing risks for relapse/reccurrence of depression. Understanding someone's interpersonal functioning is an important role in monitoring recovery from illness.

There is little in the literature comparing pre- and post-operative measures of interpersonal functioning following psychiatric neurosurgery. Here we report outcomes following anterior cingulotomy for chronic, treatment-refractory depression.

Method: The Inventory of Interpersonal Problems – 64-item (IIP-64) is a self-report measure of difficulties that people repeatedly encounter in their relationships with others. The eight scales of the IIP64 assess interpersonal problems in eight domains: Domineering/Controlling; Intrusive/Needy; Self-Sacrificing; Overly Accommodating; Nonassertive; Socially Inhibited; Cold/Distant; Vindictive/Self-Centred. The total score reflects how much difficulty a person experiences in interpersonal relationships.

We use the IIP-64 routinely to assess interpersonal functioning over time. We now report the outcomes from 15 patients who underwent anterior cingulotomy for chronic, treatment-refractory depression. The IIP-64 was completed at baseline and at 12-months following surgery. Response at 12-months was defined as ≥50% improvement on the 17-item Hamilton Rating Scale for Depression (HRSD-17).

We compared changes in scores on the IIP-64 in relation to changes in symptom burden. Scores were ipsatised by subtracting the individual's mean scores from each response on other items in the questionnaire in order to compensate for uniform response bias. Ipsatised scores on each of the IIP-64 domains were plotted pre- and post-surgery. Total T-scores at 12-months were compared between responders and non-responders. Finally, we attempted to relate change in depressive symptoms to changes in interpersonal functioning.

Result: Fifteen individuals (M:F ratio was 1:14) underwent thermal anterior cingulotomy. The mean ± SD age was 48.9 ± 8.3 years. The mean ± SD baseline HRSD-17 score was 28.5 ± 5.0. Five of the fifteen (33.3%) had previously failed to respond to a trial of Vagus Nerve Stimulation (VNS), but none had previously undergone ablative neurosurgery.

All individuals demonstrated impairments in interpersonal functioning at baseline, with mean total T-scores on the IIP-64 of 70.3 ± 7.9. As expected, depressed patients showed greatest difficulties in domains related to depression such as: Nonassertive; Socially Inhibited; and Cold/Distant.

In terms of response rate, 7/15 (46.7%) met criteria for response at 12-months. Those who responded showed a reduction in their IIP-64 Total T-score from 68.3 ± 7.4 to 56.3 ± 14.7. Non-responders showed no significant change in their scores: baseline 72.0 ± 8.3; 12-months 72.1 ± 8.3. Responders tended to show a 'normalisation' of scores in typically depressive domains, with improvements observed in domains relating to greater control and greater affiliation.

There was a robust relationship between magnitude of change on the HRSD-17 at 12-months and change on the IIP-64, with those showing greatest symptom improvement having the greatest improvement in interpersonal functioning (Pearson's $r = 0.645$; $p = 0.009$).

Conclusions: Although the sample size is relatively small, there are clear relationships between improvements in depressive symptoms and changes in interpersonal functioning. Furthermore, there is a statistically-significant relationship between symptom change and improvement in interpersonal functioning. Importantly, there was no evidence of deterioration in interpersonal functioning; even in non-responders.

At the current time, it is not possible to determine if changes in interpersonal functioning pre-date improvements in mood. However, the relationship between symptoms and interpersonal difficulties would support the hypothesis that as symptoms improve, an individual's interpersonal functioning improves.

Prospective monitoring of interpersonal functioning is, therefore, a useful tool in assessing outcome following neurosurgical treatment of depression.

#8607

Nucleus Accumbens Stimulation in Pathological Obesity – Cases of Three Patients

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Keywords: Deep brain stimulation, Obesity, Nucleus accumbens.

Introduction: We present three cases of patients with morbid obesity, treated by bilateral deep brain stimulation of the nucleus accumbens. In these cases, the starting point of illness was the operation of the craniopharyngioma with multihormonal hypothalamic pituitary deficiency.

Patients and Methods: First patient M.K. with a BMI of 52.64 (weight 150.7 kg). He was implanted stimulator for deep brain stimulation to both sides of the nucleus accumbens septum (nucleus accumbens – NACC). The procedure was performed on 06.07.2012. During hospitalization we not observed any negative consequences of stimulation, weight at the day of departure from hospital was lower by 3.5 kg.

The second patient N.Z. with severe obesity (weight 132 kg assuming the increase 168 cm) – was implanted stimulator for deep brain stimulation to both sides of the nucleus accumbens septum

(nucleus accumbens – NACC) on 02.21.2014. Surgery without complications. Good tolerance stimulation.

The thirdpatient M.K. with severe obesity (weight 138 kg assuming the increase 164 cm) – was implanted stimulator for deep brain stimulation to both sides of the nucleus accumbens septum (nucleus accumbens – NACC). Surgery without complications. Good tolerance stimulation.

Results: After a month M.K. body weight from baseline was lower by more than 7 kg. We did not observe any complications and side effects during the period of stimulation. The neuropsychological study without deviating from the norm, especially without cognitive impairment. The patient feels well, thinking about food take sick about 20% of the daily activity – previously about 80%. In the course of treatment has been interrupted twice stimulation – the first time because of the stimulator off, the second time because of damage to the connecting cables. In both situations, the patient reported immediately to the consultation feeling strong deterioration.

The second patient N.Z. feels good, thinking about food can control, not eating at night (before mandatory every 2 h). On the day of the quantity and quality of meals does not deviate from the norm, the patient no longer feels compulsion food.

The third patient N.Z. can fully control thinking about food, the patient no longer feels compulsion food.

Conclusions: In our opinion, based on the results of the patients described above, the treatment proved to be effective and safe procedure.

Radiosurgery

#8513

Diffusion Weighted Imaging of Peripheral Nerves in High Intensity Focused Ultrasound Surgery

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Keywords: Diffusion imaging, Tractography, Focused ultrasound.

Objectives: Diffusion weighted imaging (DWI) is a valuable tool for localizing white matter fibres and measuring metrics of diffusivity. Conventional imaging methods are limited in their ability to distinguish white matter tracts from surrounding tissue. Diffusion imaging and tractography algorithms can be used to overcome this limitation by visually reconstructing anatomically accurate white matter fibres. While this technique has been successfully used in the CNS, DWI of peripheral nerve fibres has been very limited, but would prove to be of value in non-invasive treatment, including focused ultrasound (FUS), particularly since DWI allows for in vivo measurement of microstructural changes following FUS. In this study we report a method of anatomically accurate DWI reconstruction of the sciatic nerve in a piglet model, followed by measurement of diffusivity metrics before and after lesioning of the sciatic nerve with FUS.

Methods: Bilateralsciatic nerves in two piglets (average weight 7.5 kg) were studied. T1 anatomical and DWI scans were acquired on a 3T MRI using a 32-channel cardiac-torso phased receive-only coil. The DWI scanning parameters included 128 diffusion directions, 1.6 mm isotropic voxel resolution, and diffusion weighting of b = 800 s/mm^2. Eddy current, motion, and fieldmap corrections were performed. A one-direction reverse phase-encoded sequence was also incorporated for correcting diffusion gradient-associated image distortions. The T1 and DWI scans were co-registered for accurate anatomical localization. Probabilistic streamline tractography was performed using MRTrix3 with the following parameters: step size 0.16 mm; stopping angle 30 deg; stopping and initial fibre orientation amplitude 0.1; generated tracks 1000. Fibre tracts were used to target the sciatic nerves in all subjects using an MR-guided FUS system. Targeted regions were sonicated once per nerve with the following parameters: treatment cell diameter 8 mm; exposure time 27 s; input power range 50–110 W. A region of interest (ROI) based analysis was performed in order to measure scalar diffusion metrics of fractional anisotropy (FA), radial (RD), axial (AD), and mean (MD) diffusivities. Five cross-sectional ROIs (3.2 x 3.2 x 1.6 mm^3) were placed along the sciatic nerve covering the region targeted by the FUS beam. Comparisons were performed across nerve segments before and after treatment.

Results: The tracts of all sciatic nerves were successfully imaged both before and after treatment. Tracts extended from the spinal cord dorsal root ganglion past the distal head of the ipsilateral femur. Measurement of ROI diffusion metrics in the targeted segments demonstrated that, following treatment, there was a significant decrease in FA and significant increases in MD and AD ($p < 0.05$). An increase in RD was also observed but it failed to reach statistical significance ($p = 0.055$). Histological analysis confirmed FUS lesions covering the nerve as well as surrounding hamstring muscle.

Discussion: Using the described imaging protocol, we were able to consistently reconstruct the sciatic nerve in piglets both before and after treatment with FUS. The tracts of the sciatic nerve could be easily distinguished from surrounding blood vessels, fat, muscle, and other tissue which can otherwise obscure accurate target identification. Post-treatment subjects exhibited decreased FA and increased diffusivities at the treatment site. This is indicative of the thermal breakdown of axonal nerve fibres as the directionality of water diffusion becomes more isotropic following FUS sonication. DWI and tractography algorithms have thus been shown to be effective tools for visualizing white matter structures for FUS targeting and for assessing the microstructural changes that occur following FUS treatment.

Spasticity

#8420

Management of Life-Threatening Complications of Intrathecal Baclofen Therapy

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Keywords: Baclofen, Spasticity, Intrathecal, Complications.

Intrathecal Baclofen therapy is a well-recognized safe and effective treatment modality in selected patients with medical refractory spasticity. The medicine (β-[4-chlorophenyl]-GABA) is delivered through a programmable pump implanted subcutaneously and connected with a close system to the subarachnoid space. The pump is usually filled 2–4 times per year. Sudden under or over dosing of the Baclofen drug delivered to the intrathecal space may lead to serious and possibly fatal outcome. In this presentation the author will describe his experience in managing cases suffering serious complications of intrathecal baclofen therapy treated in his center. These include cases of Baclofen deprivement and overdosing. The presentation shall discuss issues of preventing, early recognition and management of these serious and can be fatal complications.

#8499

A New 'Hybrid' Pump for Intrathecal Baclofen Therapy

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Keywords: Spasticity, Intrathecal baclofen therapy, Programmable pump, Hybrid pump.

Objectives: Presentation of a case series of 3 patients suffering from intractable spasticity, treated with intrathecal baclofen therapy. A new 'hybrid' pump (Siromedes 20 ml, Tricumed) was implanted in all patients, during the period from November 2015 to January 2016.

Methods: a) A 30 year old female patient developed spastic right hemiplegia after a road traffic accident in 2004. She was treated with intrathecal baclofen therapy until the depletion of her programmable pump. In November 2015 she underwent surgical substitution of her previous pump with the new 'hybrid' pump. b) A 68 year old male patient developed spastic right hemiparesis after several ischemic episodes. He was receiving intrathecal baclofen therapy with a programmable pump since 2009. His old pump was depleted and replaced with the new 'hybrid' pump. c) A 17 year old male patient was suffering from severe spastic tetraparesis due to cerebral palsy. He underwent implantation of the new 'hybrid' pump.

Results: The post-operative period was smooth for all three patients, with spasticity efficiently alleviated immediately after the initiation of baclofen therapy. The new baclofen pump represents a unique 'hybrid' mode of function, since it can be programmable for at least 8 years and thereafter continues to operate for a long period as a constant flow pump.

Conclusions: The new 'hybrid' pump appears to be a safe and efficient alternative for intrathecal baclofen therapy. All 3 patients had an uncomplicated follow up period of 5 months or more. Longer follow-up periods and a larger patients sample are necessary for conclusive results.

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