

Epilepsy

Proton MRS in Patients Suffering of Medically Refractory Epilepsy due to Mesial Temporal Sclerosis

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Introduction: Proton MR Spectroscopy (1HMRS) has been widely employed in the preoperative evaluation of patients with medically refractory epilepsy of mesial temporal origin. Numerous studies have evaluated 1HMRS role in assessing mesial temporal lobe biochemical profile in patients with medically intractable epilepsy. In our current communication we present our spectroscopic findings of temporal pole in patients with mesial temporal sclerosis (MTS).

Methods: A total of 50 patients (32 M & 18 F) suffering of medically refractory epilepsy due to MRI proven, unilateral MTS were included in our prospective study. All participants underwent preoperatively 1HMRS of the mesial structures and the temporal poles. The concentrations of N-acetyl-Aspartic acid (NAA), Choline (Cho), and Phosphocreatine/Creatine (PCr/Cr) were measured. Histopathological findings of the resected temporal poles were compared to the preoperative spectroscopic abnormalities.

Results: Mesial temporal abnormalities (increased Cho and PCr-Cr and decreased NAA concentrations) were evident in all patients on the affected side, but in only 23/50 (46%) on the opposite to the MTS side. Spectroscopic abnormalities of the ipsilateral temporal pole were present in 38/50 (76%), while the contralateral temporal pole had abnormal spectroscopic profile in 3/50 (6%). Temporal pole histopathological abnormalities were evident in 35/38 (92.1%) of the patients with spectroscopic abnormalities, while none of the patients with normal temporal pole spectroscopy had any histopathological abnormalities.

Discussion: Temporal pole 1HMRS may reveal extensive, irreversible neocortical abnormalities associated with MTS.

Conclusions: Temporal pole 1HMRS may provide valuable information regarding any neocortical involvement in cases of MTS and may help selecting the most suitable surgical approach in each case.

Epilepsy

MRI-Guided Stereotactic Laser Thermal Amygdalohippocampotomy (SLTAH) for Mesial Temporal Epilepsy

Jon T. Willie

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INTRODUCTION:

Real-time magnetic resonance imaging (MRI)-guided stereotactic laser thermal ablation of mesial temporal lobe structures may be a safe and effective minimally-invasive alternative to open resection for mesial temporal lobe epilepsy (MTLE).

METHODS:

Nine procedures were performed in eight consecutive adult patients (ages 18-64) with intractable MTLE. A saline-cooled fiber optic laser applicator (Visualase, Inc.) targeting anterior amygdalohippocampal structures from an occipital trajectory was inserted utilizing a stereotactic frame under general anesthesia. Laser energy was delivered during continuous MR imaging. Temperature-sensitive phase images and estimates of thermal damage during heating were superimposed on anatomical images in real-time. Standard MRI scans were obtained immediately post-procedure, with reimaging planned at 6 months. Prospective baseline and post-operative seizure diaries, quality of life measures, and neuropsychometric testing are being performed.

RESULTS:

In the first two patients, ablations limited to the parahippocampal gyrus did not yield seizure-freedom. All subsequent procedures produced technically successful anterior amygdalohippocampal ablations. Of these, two patients with mesial temporal sclerosis (MTS) are Engel class I at 3-6 months, whereas two patients without MTS are not. Outcomes for the remaining recent ablations await determination. Of the original two patients, one underwent a repeat procedure, resulting in successful amygdalohippocampotomy, but also a visual field deficit.

DISCUSSION:

SLTAH is technically feasible. Very preliminary results indicate that seizure outcomes might possibly differ in patients with and without MTS.

CONCLUSIONS:

The safety and efficacy of SLTAH, an appealing minimally-invasive approach, needs to be carefully evaluated with a larger cohort over periods of at least one year.

Epilepsy

Middle Short Gyrus of the Insula Implicated in Speech Production: Intracerebral electric Stimulation

Afif AFIF

Afif Afif (none), Dominique Hoffmann (none), Lorella Minotti (none), Philippe Kahane (none)

Afif Afif 1, 2; Lorella Minotti 3; Philippe Kahane 3; Dominique Hoffmann 4

Introduction

The data of this study suggests the involvement of the upper middle short gyrus in speech production.

Methods

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

Results

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

The data suggest the involvement of the middle short gyrus of the insula in the procedures of language.

Discussion

This study provides evidence that the middle short gyrus of the insula responds to ES producing speech disturbances.

Conclusions

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

Epilepsy

Robotic Placement of Intracranial Depth Electrodes for Long-Term Monitoring: Utility and Efficacy

Gwyneth Hughes

Gwyneth Hughes (none), Jorge Gonzalez-Martinez (none), Juan Bulacio (none), Sumeet Vadera (none)

Introduction: To investigate the utility and efficacy of robotic stereotactic assistance in the placement of intracranial depth electrodes for invasive monitoring in patients with intractable focal epilepsy.

Methods: From November 2010 to January 2012, 33 patients underwent robotic assisted stereotactic placement of depth electrodes for long term monitoring. All patients were considered to have medically refractory focal epilepsy. ROSA device (Medtech, Montpellier, France) was used for planning and implantation guidance in all procedures. Implantation time, efficacy in mapping the epileptogenic zone, and complications were analyzed.

Results: Mean age was 30 years-old (4 to 59 years). Mean duration of the epilepsy syndrome was 13.8 years (0.83 to 52 years). 438 electrodes were implanted. Proprietary ROSA software facilitated an efficient trajectory planning stage. 19 patients underwent unilateral implantation. 14 patients underwent bilateral implantation. The mean OR time during implantation was approximately 2 hours. The robotic implantation was successful in localizing the electrophysiological epileptogenic zone in 31 patients (94%). Asymptomatic subdural hemorrhage occurred in 2 patients. A small intracranial contusion resulting in temporary leg weakness occurred in 1 patient. The complication rate per electrode was 0.68%.

Discussion: Robotic assistance provided a highly efficient and safe electrode implantation technique. A randomized trial comparing standard methods of implantation versus robotic implantation is necessary to confirm these conclusions.

Conclusion: Robot assisted placement of intracranial depth electrodes streamlines the implantation process, without sacrificing safety, in patients with intractable focal epilepsy.

Epilepsy

Amygdalo-Hippocampotomy, surgical technique and clinical results

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Introduction:

Since 2007 we performed selective amigdalo-hippocampotomy, with hippocampal disconnection instead of removal, for treatment of refractory temporal lobe epilepsy (TLE) due to mesial temporal lobe sclerosis (MTLS). The surgical technique and results are presented.

Method:

21 patients (14 females) aged 20-58 years (mean:41y) were operated with this technique: selective ablation of lateral amygdala plus peri-hippocampal disconnection (2/3 anterior on dominant hemisphere), including the para-hippocampal gyrus. In 20 patients the follow-up time was 24- 44 months (average: 32 months).

Results and Discussion:

Operative time was reduced with this technique in 30 minutes (15 %) in average and no risk due to intra-subarachnoidal vascular dissection was present. The histopathology diagnosis was MTLS in 20 patients (in one patient material was lost). Surgical outcome for epilepsy (at 2 year follow-up): good/very good in 19 patients (95%), with Engel Class I-A in 15 (75%) and II-A in 4 (20%); bad in 1 patient (5%) in Class IV (patient with an ipsilateral posterior temporal focus appeared later). Surgical morbidity: one patient with hemiparesis (hypertensive haemorrhage 12 hours after surgery), 2 with memory worsening, 3 with quadrantanopia. In 3 cases late psychiatric depression developed.

Conclusions:

Advantages: Amygdalohippocampotomy is safer and as effective as amygdalohippocampectomy, and is a time-saving procedure.

Disadvantages: Some isolated epileptiform EEG activity may be seen post-surgically. The surgical technique is video-illustrated in the presentation.

Epilepsy

Magnetic Resonance Temperature Imaging (MRTI) of Laser Ablation for Hippocampal Sclerosis (HS)

Chengyuan Wu

(Other Financial or Material Support, Company: Materials provided by Visualase, Inc. (Houston, TX))

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INTRODUCTION: Patients with unilateral Hippocampal Sclerosis (HS) represent the most suitable candidates for epilepsy surgery; but risk of cognitive decline and invasiveness of open craniotomy is a limiting concern. Minimally invasive stereotactic laser ablation (SLA) enables precise ablation of seizure foci with sparing of eloquent neocortical structures.

METHODS: Under general anesthesia, patients (n=5, ages 16-58, 2-12 seizures/month) were placed in a stereotactic (CRW/Leksell) head frame and cranial access was obtained via a 3.2mm twist drill hole. Frame-based navigation was used to introduce an MR-compatible laser applicator to the amygdalohippocampal complex from a temporo-occipital trajectory. An FDA-cleared surgical laser ablation system (Visualase, Inc., Houston, TX) was utilized. After a test dose of 3-4W for 15-45 seconds confirmed applicator position, 2 exposures of 10-12W for 90-130 seconds were used to ablate the amygdalohippocampal complex. Temperature was monitored and safety limits (50°C) were placed near critical structures. Post-ablation T1-weighted gadolinium series were acquired.

RESULTS: The trajectory used was appropriate for controlled thermal ablation of desired structures and volumes, which was confirmed by MRI. No surgical complications and no neurocognitive deficits were noted acutely. Average length of stay was 1 day. Patients have been seizure free at last follow-up (2-12 months post-procedure).

DISCUSSION: Even with high success rates of traditional epilepsy surgery, it is vastly underutilized due to its associated morbidity. SLA of HS may represent a minimally invasive alternative for suitable candidates.

CONCLUSIONS: Initial results demonstrate SLA to be a safe for destruction of epileptogenic foci in patients with medically intractable and HS.

Epilepsy

Minimally Invasive Stereotactic Laser Ablation of Hypothalamic Hamartomas (HH)

Daniel J. Curry

(Stock or Shareholder, Company: Visualase, Inc. (Gowda, McNichols, Shetty))

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INTRODUCTION: Surgical intervention for HH has been limited due to modest outcomes (37- 50% seizure freedom) and associated surgical morbidity (7-33% permanent). Seizures are primarily gelastic, medically intractable and are frequently associated with intellectual deterioration and disordered behavior. We report seizure outcomes after completion of minimally invasive MRI-guided real time stereotactic laser ablation (SLA).

METHODS:

An MR-compatible laser catheter (1.6mm dia) was navigated to the HH with frame-based stereotaxy and a 3.2mm twist drill hole (n=3, age range 5-15 years). An FDA-cleared laser surgery system (Visualase, Inc., Houston, TX) was utilized to monitor the ablation process with real-time MRI thermometry. After confirmation test at 3W, higher doses of 6-10 W for 50-120 seconds were used to ablate the HH. Temperature limits were set to protect nearby vital structures.

RESULTS:

The average OR time was 4.1 hrs and average MR time was 1.4 hrs. There were no permanent surgical, neurological, visual, or endocrine complications, including no diabetes insipidus. One patient had temporary short term memory deficit, and two patients had temporary increase in appetite. At last follow-up (11, 7 and 5 months), complete seizure freedom was observed in all 3 patients.

DISCUSSION:

SLA was demonstrated to be a safe and effective minimally invasive tool to destroy epileptogenic HH. Seizure freedom was achieved without permanent surgical morbidity. Short ablation times (60-120 seconds) and real-time MRI thermometry enabled protection of adjacent critical structures.

CONCLUSIONS:

Minimally invasive MRI-guided real time SLA may present a safe and effective surgical option in treating HH related epilepsy.

Epilepsy

Treatment of medically intractable partial seizures with responsive stimulation: Final results of th

Ryder Gwinn MD

(Stock or Shareholder, Company: Nevro Corporation), (University Grants/Research Support, Company: ANS), (University Grants/Research Support, Company: St. Jude), (University Grants/Research Support, Company: NeuroPace, Inc)

Martha J. Morrell MD (Disclosure: Employee [any industry] Company: NeuroPace), Ryder Gwinn MD (Disclosure: University Grants/Research Support Company: St. Jude), Ryder Gwinn MD (Disclosure: University Grants/Research Support Company: ANS), Ryder Gwinn MD (Disclosure: University Grants/Research Support Company: NeuroPace), The RNS System Investigators (Disclosure: University Grants/Research Support Company: NeuroPace)

Introduction: The RNS[®] System is an investigational cranially implanted responsive neurostimulator evaluated as an adjunctive therapy in individuals ≥ 18 years of age with medically refractory partial onset seizures from ≥ two foci.

Methods: 191 subjects across 32 centers were implanted and randomized 1:1 to active or sham responsive stimulation. Efficacy was assessed over a 12 week blinded period and a subsequent 84 week open label period (OLP; all subjects received stimulation).

Results: The average subject took 2.8 AEDs/day and had 1.2 seizures/day; 32% were previously treated with cortical resection and 34% with a VNS.

Seizures were significantly reduced from baseline during the blinded period in the active (-37.9%, N=97) compared to the sham group (-17.3%, N=94; p=0.012, GEE). In the OLP, the median % seizure reduction improved over time (44% at 1 year and 53% at 2 years, p<0.001). Verbal and visual-spatial function, memory, mood, and quality of life (QOL) were significantly improved.

Adverse events (AEs) were not different between active and sham groups; rates did not increase over time. AEs affecting > 5% of subjects were EEG monitoring (7.3%) and increase in complex partial seizures (5.2%). Deaths were 4 SUDEP events, 1 suicide and 1 lymphoma.

Discussion: Responsive stimulation reduced seizures without increasing AEs compared to sham stimulation. The seizure reduction was sustained.

Conclusions: Treatment with the RNS System has the potential to reduce partial seizure frequency and improve QOL in persons with epilepsy intractable to medications and often to surgery and VNS, without mood or neuropsychological risks.

Epilepsy

Surgical Treatment of the Patients with Rasmussen's Encephalitis

Guoming Luan

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Introduction: To describe the clinical, electrophysiologic, neuroradiologic, and histologic findings of patients with Rasmussen encephalitis (RE) and to evaluate the outcome of their surgical treatment.

Methods: This report was based on a consecutive series of 34 patients affected by RE studied and operated on at the Department of Functional Neurosurgery, Sanbo Brain Hospital from April 2004 to December 2010. The age at surgery was from 2.8 years to 17 years. 34 RE patients were confirmed by presurgical evaluation including semiology, magnetic resonance imaging (MRI), interictal/ictal scalp video-electroencephalography (VEEG), intracranial recording and biopsy.

Results: 19 functional hemispherectomy (FH), 9 anatomical hemispherectomy (AH), 6 hemispherotomy procedures were undertaken. According to Engel's criteria, 28 patients (83%) achieved an Engel Class I status. 1 patient showed contralateral seizure after AH and be diagnosed as bilateral RE. All of the patients excepting one bilateral RE had increases in cognitive abilities, behavior, and quality of life after the surgery.

Discussion: Hemispherectomy and hemispherotomy may be the only and very effective therapy to achieve seizure freedom in RE patients, seizure freedom rates is 83%. Hemispheric surgeries should be performed before a serious neurological deficit appearance. After operation, most patients are able to walk without the use of assist device, but the fine hand movements are lost.

Conclusion: Hemispherectomy and hemispherotomy were confirmed as both beneficial procedures in controlling seizures and improving quality of the life in cases with RE.

Epilepsy

Thalamic Specific Nuclei DBS for Refractory Partial Epilepsy

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Barbara A. Morais (none), Dacio A. Pereira (none), Paulo C. Ragazzo, MD, PhD (none)

Introduction: Refractory partial epilepsy with motor or sensory symptoms may present an ictal onset zone coincident with primary sensorimotor cortex, preventing cortical resection for seizure control. Thalamic AN and CM-DBS have been used to control partial and generalized seizures. Considering the projections of the motor and sensory thalamic nuclei to the sensorimotor cortex, we performed combined AN and Vim-DBS to treat refractory motor seizures in a patient already submitted to a partial resection of a focal cortical dysplasia and still presenting persistent seizures.

Methods: a 40-year-old female patient presenting with long-term refractory asymmetrical (lateralized to the right side) tonic and hemiclonic seizures, previously submitted to partial resection of a focal cortical dysplasia encroaching on the left motor cortex, underwent stereotactic unilateral AN and Vim-DBS. Preoperative evaluation: MR, VT-EEG, PET-CT, and neuropsychological assessment. Target localization was confirmed with MER. Intraoperative Vim stimulation consistently reduced the burst of spikes recorded through intraoperative scalp EEG.

Results: There were no immediate postoperative complications. The sleep-wake transition seizures were reduced from many clusters of approximately 10 seizures each to none or a single cluster of 2-3 very mild seizures. There was no additional neurologic deficit related to thalamic stimulation. So far, only the Vim lead was activated. The following parameters showed the best response: monopolar stimulation, 2.7V, 25Hz, and 120 μ s.

Discussion/Conclusions: Vim-DBS may have a positive effect in the control of partial motor seizures related to ictal onset in the motor cortex. One may assume that VC-DBS may show similar results on partial sensory seizures.

Epilepsy

Epilepsy Outcome After Cerebral Cavernous Malformations Treatment

Faisal Al Otaibi, MD

A. Al Semari, MD (none), Diya Sabbagh (none), Faisal Al Otaibi, MD (none), Nasser Alohalay, MD (none)

Introduction: Cerebral Cavernous Malformations (CCMs) are commonly associated with seizure disorder. In this study, we analyze the predictors that might impact the chance of seizure freedom after CCMs treatment.

Methods: Subsets of 19 patients with CCMs were retrospectively analyzed. Seizure frequency pre and post-treatment was measured. The magnetic resonance imaging (MRI) features was assessed in terms of CCMs location, size and hemosiderin thickness around the lesion.

Results: The group of patients includes eleven females and eight males with age ranging between 5 and 62 years (mean 29.2, SD 12.3). The mean duration of epilepsy was 12.6 years ranging between 4-36 years. CCMs were located in the temporal lobe in 4 patients, perirolandic area in 5, multiple in 4, and other locations in 5. The average CCMs size was 2 cms with average hemosidren thickness of 3 mms. Thirteen patients underwent surgical resection (lesionectomy, lesionectomy plus extensive corticectomy, and lesionectomy with temporal lobectomy). Two patients underwent radiosurgery using Cyberknife with a limited benefits. Overall, Eight patients became seizure free (8/13, 61%), 3 had partial improvement, and 2 had worsening of seizure frequency. The important factor that was associated with seizure freedom is lesionectomy with extensive corticectomy or lobectomy. Temporal and perirolandic location was associated with more intractable epilepsy.

Discussion: CCMs with prolonged epilepsy duration may need an extensive corticectomy or lobectomy in addition to lesionectomy

Conclusions: Lesionectomy with extensive corticectomy or temporal lobectomy was found to be an important factor for seizure freedom after CCMs treatment.

Epilepsy

NeuroPace Cortical and Depth Impedance Changes Differ

Karl Sillay

ASSFN Abstract

AUTHORS:

Karl Sillay MD; Heather Rusk MD; Joseph Hippensteel MS; Justin Williams PhD, and Paul Rutecki MD

RATIONALE:

Many patients suffering from epilepsy continue to have seizures in spite of medical management. A new technology involving intracranial neurostimulation, the Neuropace RNS[®] System, offers an alternative surgical option for patients with refractive epilepsy. However, little is known about the impedance trends in the device after implantation and how those values relate to the long-term effectiveness.

METHODS:

To determine any differences in cortical and depth electrodes used in the device, we measured impedances for the Neuropace RNS System electrodes following implantation for a 20 month period. The values were later retrieved by retrospective review and the cortical versus the depth electrode values were compared.

RESULTS:

The cortical electrodes showed an initial increase in impedance in the first 30 days post-implantation, while the depth electrodes showed an initial decrease. The impedances of both electrodes then leveled off to relatively stable values for the remainder of the time period. However, following the initial 30 day period, cortical electrodes showed overall greater impedance levels.

CONCLUSIONS:

Impedance stability varies between the cortical and depth electrodes. As the differences in impedance values may determine the most beneficial mode of stimulation, further investigation is needed. Also, further study is warranted to determine if the stability of impedance relates to seizure outcome over time, and to determine the mechanism of impedance change between the sites of electrical stimulation.

Epilepsy

fMRI TO LOCATE CORTICAL ELOQUENT AREAS IN EPILEPSY SURGERY CANDIDATES: COMPARISON TO BRAIN MAPPING W

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Objective: To determine whether the eloquent area identified by fMRI is concordant with that identified by brain mapping using cortical stimulation.

Methods: Patients who required implantation of cortical grids on eloquent areas for continuous EEG monitoring underwent presurgical fMRI and postsurgical extra operatory brain mapping with cortical stimulation. A postsurgical structural MRI was obtained and reconstructed with Eclipse software in order to determine the position of the grid. By image fusion, the location of the grid contacts where the eloquent area was identified was compared to the location of the eloquent area by fMRI.

Results: Six eloquent areas were compared, five motor and one for language (Wernicke area). In all motor areas fMRI and brain mapping were concordant in the identification of the eloquent area. For Wernicke area both methods were concordant in not identifying it on the left side (the patient had right language dominance). This patient underwent left temporal lobectomy, no postsurgical neuropsychological sequelae were present.

Discussion: In this study fMRI and brain mapping with cortical stimulation were 100% concordant in identifying eloquent areas. Isometric sequences with coronal slices were the best for 3D reconstructions of structural MRI. An MRI processing protocol has been established and will be used for all future cases. Further study, especially for language areas, is still necessary.

Epilepsy

Frameless Stereotactic Guided Radiofrequency Thermal Ablation of Hypothalamic Hamartomas

Amir Kershenovich

(Other Financial or Material Support, Company: FHC)

Frank Gilliam (none), Matthew Eccher (none), Steven Toms (none)

Introduction Hypothalamic hamartomas(HH) are associated with pharmacoresistant gelastic seizures(GS). Besides surgical tumor removal, stereotactic-radiofrequency-thermocoagulation(SRT) has been used successfully.

Objectives We present the first two cases of HH with GS treated using a frameless SRT system.

Methods Report of two cases: a 32 year old female(patient#1) with GS for 27 years (>100 events/day), and a 53 year old male(patient#2) with GS for 47 years (>30 events/day). The FHC-StarFix-micro-targeting frameless-stereotactic platform was used together with the Cosman/Radionics radiofrequency generator to ablate multiple areas of the hamartoma/hypothalamic interface with two different diameter electrodes (1.1 and 1.6mm by 4mm length).

Results For patient 1 we used 9 different targets in 9 different passes using 1 offset. For patient 2 we first performed an invasive EEG by passing a 4 contact depth electrode into the HH. No epileptic spikes and only normal waves were seen. Then 5 targets through 5 different passes were made using 2 offsets.

There were neither intra or postoperative complications and/or side effects.

Both patients had more than 75% improvement on their latest follow up at 14 and 6 months postoperation respectively.

Discussion Kameyama et al. reported that in their series of 25 patients, SRT required 1 to 8 passes (mean 3.8) for 1-18 targets (mean 7.2). In 6 patients, the GS relapsed within 4 months. They reported 0% permanent complications and overall 76% Engel I outcomes for all seizures and 92% for GS control.

Conclusions The FHC StarFix stereotactic platform is a safe, comfortable and effective means to ablate an Hypothalamic Hamartoma.

Epilepsy

Vagus Nerve Stimulation for Epilepsy: A Comparison of Outcome at One Year and Two Years Intervals

Faisal Al Otaibi, MD

A. Abujaber, RN (none), A. Semari, MD (none), Faisal Al Otaibi, MD (none), S. Baz, MD (none)

Introduction: Vagus nerve stimulation (VNS) therapy reduces seizures in certain patients with pharmacoresistant epilepsy who are not candidates for resective surgery. This study was conducted to compare the outcome of VNS therapy at one year and two years intervals.

Methods: Aretrospective analysis of 24 patients who received VNS therapy was conducted. Seizure frequency was measured before therapy, after one year of therapy, and at two years of therapy using seizure diary. No changes in antiepileptic regimen after VNS implantation. VNS programming was standardized for all patients groups with adjustment based on tolerance and side effects. The response to VNS was defined as > 50% reduction of baseline seizure frequency

Results: A group of 20 adults and 4 pediatrics were identified. At one year of VNS therapy 33% (n = 8) were considered responders (> 50% reduction of seizure frequency). At two years of VNS therapy 41% (n =10) were considered responders. Non of the patients developed worsening of seizure. One patient underwent device removal after 19 months of therapy due to no benefit and patient request. Overall, the adverse effects (hoarseness, coughing) induced by stimulation are mild.

Discussion: VNS is more efficacious in reducing epilepsy at two years of therapy as compared to one year. This indicates accumulative effect of chronic neurostimulation on epilepsy.

Conclusion: VNS therapy has more effect on seizure reduction at two years of therapy. It is a well tolerated treatment modality for epilepsy.

Epilepsy

Vagus Nerve Stimulator for Epilepsy: A Comparison of Outcome at One and Two Years Intervals

Faisal Al otaibi, MD

A. Abujaber, RN (none), A. Semari, MD (none), S. Baz, MD (none)

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Movement disorders

DTI and Colored FA Analysis of the CM-Pf and ALIC Targets

Mark Sedrak

Arsani William (none), Gary Heit (none), Ivan Bernstein (none), Mark Sedrak (none)

Introduction:

Two patients with successful treatment of coexisting Obsessive-Compulsive Disorder (OCD) and Tourette's Disorder were analyzed with diffusion tensor imaging (DTI) and colored fractional anisotropy (FA).

Methods:

Targets for deep brain stimulating electrodes were the anterior limb of the internal capsule (ALIC) and centromedian-parafascicular (CM-Pf) nucleus of the thalamus. Image fusion of pre- and post-op studies were carried out, stereotactic trajectories incorporated, with regions of interest (ROI's) around presumed zones of activation (ZOA) in the region of active contacts.

Results:

Colored FA and DTI mapping demonstrated very characteristic image findings for the intended targets. CM-Pf target contained a specific color pattern in the thalamus, the active contacts of which were also embedded in the ventral oralis nucleus. Projections including prefrontal projections, supplementary and primary motor regions. The ALIC was clearly involved with many pathways including anterior commissure, orbitofrontal, uncinate fasciculus and dorsal brainstem projections.

Conclusions:

This is the first report of both ALIC and CM-Pf being used for the treatment of simultaneous diseases. Different pathways exist that may explain the dual role these targets play in their respective disease processes. This appears to be an effective treatment and may be considered in severe refractory cases.

Movement disorders

Neuronal Degeneration Following Deep Brain Stimulation Insertion in Primates

Omar Zalatimo

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Introduction:

The nature of Deep Brain Stimulation requires passage of wires through neural tissue. Studies in rodents have shown placement of catheters can cause damage to surrounding tissue. This has not been demonstrated in higher animals. The purpose of this study was to investigate the pathological effect of placing electrodes in deep brain nuclei of primates.

Methods:

Two Macaques underwent implantation of a unilateral silicone catheter. The subthalamic nucleus was localized using a preoperative MRI and an atlas. The catheter was guided to the target utilizing a stereotactic frame. Unilateral placement allowed the contralateral hemisphere to serve as the control. The brains were harvested and preserved at two weeks. Samples were stained for axon degeneration, evaluated microscopically and compared to the control side for each primate.

Results:

Axonal degeneration was observed, at the insertion site and to a lesser extent in the ipsilateral internal capsule. Unexpectedly, axonal degeneration was seen in the corresponding contralateral cortex as well as in the corpus callosum and, to a lesser degree in the temporal lobe, bilaterally.

Discussion:

These preliminary findings suggest that passage of devices through neural tissue has the potential for wide ranging axonal degeneration, which raises the possibility that placement of electrodes may carry more impact than previously believed. This would potentially favor minimizing number of passes during lead placement.

Conclusion:

The widespread effects demonstrated raises the possibility that affecting one nucleus with DBS may affect a wider region in the brain than previously believed, though further studies are needed for confirmation.

Movement disorders

Stimulation of the STN in Parkinson's disease (PD) alters the network for speech production.

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Introduction

The effects of deep brain stimulation (DBS) of the subthalamic nuclei (STN) on brain activity are poorly understood. Therapeutically effective, STN-DBS can have adverse effects on speech. The effects of STN-DBS on speech was studied with positron emission tomography (PET).

Methods

Regional cerebral blood flow (rCBF) was studied (H215O PET) in seven PD subjects with bilateral STN-DBS and seven PD subjects without STN-DBS during speech. Regression analysis was used to predict speech rate from rCBF.

Results

Normally an inverse relationship between the left inferior frontal gyrus (IFG) and the right caudate nucleus predicts speech rate. These regions predict rate in PD as well, but the left IFG is abnormal, having a negative rather than a positive relationship with rate. In PD with STN-DBS on, the inverse relationship between the left IFG and the right caudate is re-established. However, bilateral STN-DBS also produces a symmetrical rCBF pattern. As speech is normally left lateralized, we calculated an IFG laterality index and examined its relationship fluency. Increased left-lateralization was correlated with higher word counts in conversational speech [$r = 0.867$; $p = 0.015$].

Discussion

STN-DBS has a positive effect in reinstating an inverse relationship between the left IFG and right caudate, but a negative effect in introducing a bilateral rCBF pattern. This may account for the difficulty with speech reported by some after DBS. The study is ongoing.

Conclusions

STN-DBS appears to normalize a cortical-subcortical relationship during speech, but also introduces bilaterality, which interferes with fluency. [NIDCD R01DC7658].

Movement disorders

Relative locations of 3D probabilistic maps of efficacy, paresthesia and dysarthria for ET Vim-DBS

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Introduction: Paresthesias and dysarthria can impact the effective use of Vim-DBS for tremor control. We present high resolution, 3D surfaces that encompass regions where tremor reduction, paresthesia, and dysarthria were observed in patients undergoing left Vim-DBS. This is the first time that relative locations of efficacy and adverse effects populated using high accuracy 3D non-rigid registration are being reported.

Method: From essential tremor patients undergoing left Vim DBS, we used 640 stimulation points (87 cases) resulting in at least 50% reduction in tremor (efficacy), 200 points (52 cases) causing paresthesia, and 84 points (27 cases) causing dysarthria intraoperatively. The points were mapped onto an averaged MRI brain atlas using previously published non-rigid registration. 3D population maps were built and overlaid on the atlas MRI along with segmented thalamic nuclei from a histological atlas.

Results: The highest probability for tremor reduction correlated with the inferior-lateral margin of Vim. A discrete area of somatic paresthesia was located inferior and posterior to the efficacy map at a distance of 3.67 mm. Dysarthria was noted to overlap with efficacy, although slightly posterior and inferior, 1.24 mm away.

Discussion: The precise location of these maps corresponds to our anatomical understanding of the thalamic sub-divisions. High probability paresthesias were well localized in Vc and distinct from tremor control. However, dysarthria in the left thalamus appeared to be interleaved with tremor control.

Conclusion: While paresthesias are logically located in a discrete area posterior to tremor control, dysarthria may be unavoidable in patients undergoing left Vim DBS implants.

Movement disorders

Impact of Impedance Changes on Stimulation Estimates in a Pre-Clinical Model for DBS

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Introduction: Most clinical deep brain stimulation (DBS) systems deliver stimulation using a voltage-controlled pulse generator. For these systems, the amount of current delivered at the electrode will be affected by the impedance of the electrode. If the impedance of the electrode varies, then the current delivered through the electrode will also vary, and thus the voltage distribution generated in the target neural tissue will vary.

In this report we demonstrate that impedances do change over time in a preclinical model of DBS, and these changes are influenced by a number of variables. We also visualized the changes in Stimulation Estimates (SE) due to impedance changes with voltage and current controlled systems.

Methods: Thirty (30) pigs were implanted with bilateral DBS leads for either 30 days or 180 days. Impedance measurements were taken repeatedly throughout the study. SEs were created using Finite Element (Comsol 4.2a) and axon cable (NEURON 7.2) models.

Results: Impedances varied over time, even though stimulation parameters remained unchanged. SEs show changes in activated volumes due to impedance changes.

Discussion: Previous researchers (Lempka et al, 2010) have proposed that instability in impedances could be partially responsible for the frequent need to reprogram stimulators in DBS patients. The SEs observed in this study are consistent with this hypothesis.

Conclusion: The impedance instability observed in this animal model would be expected to result in changes in the activated volume for voltage-controlled DBS systems, while current-controlled pulse generators may deliver stimulation that is less affected by changes in impedance.

Movement disorders

Levodopa Induced Beta Band Suppression Correlates Better with Bradykinesia Assessed Using a V-M Task

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Introduction: Local field potentials (LFP) recorded from deep brain stimulation (DBS) electrodes implanted in the subthalamic nucleus (STN) provide a unique opportunity to investigate neural activity in human basal ganglia circuits. Recently, much interest has focused on the relationship between LFP beta band (14-30Hz) and bradykinesia, and excessive synchronization of STN beta band activity has been correlated with bradykinesia in Parkinson's disease (PD). Here we investigated the relationship between LFP beta band power and objective measurement of bradykinesia.

Methods: We recorded LFPs from implanted DBS electrodes 3 weeks after DBS surgery, in 5 PD patients. Patients executed arm movements during a visuo-motor task. Hand position and movement duration were assessed using a stylus on an external computer tablet. Performance was assessed before (Off) and after (On) levodopa administration. The ratio of beta power between On and Off-states in the baseline was computed in decibel (dB) scale.

Results: All subjects performed significantly faster arm movements after levodopa administration ($p=0.044$, mean \pm std; Off=1s \pm 0.5; On=0.59s \pm 0.11). The beta band power was significantly suppressed in the on-state ($p=0.0298$, -3.6dB \pm 3). This suppression significantly correlated with the movement time difference between off and on-states ($r=0.78$, $p<0.01$) whereas the correlation with UPDRS motor score was $r=0.59$ ($p=0.02$).

Discussion: Our results indicate that amplitude suppression of the beta band is a better predictor of the computerized measurement of movement time differences between Off and On-states.

Conclusion: Levodopa-induced amplitude suppression of LFP beta oscillations significantly correlates with objective computerized measurement of bradykinesia—potentially yielding a new technique for bradykinesia assessment.

Movement disorders

Long-Term Quality of Life Following Unilateral Thalamic Deep Brain Stimulation for Essential Tremor

Jules M Nazzaro, MD

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Introduction: The purpose of this study was to evaluate short and long-term benefits in quality of life (QoL) after unilateral deep brain stimulation (DBS) for essential tremor (ET).

Methods: Patients who received unilateral DBS of the ventral intermediate thalamic nucleus (VIM) from 1997 to 2010 and had at least one follow-up evaluation at least one year after surgery were included. QoL was assessed with the PDQ-39 and tremor with the Fahn-Tolosa-Marin tremor rating scale (TRS) prior to surgery and postoperatively.

Results: Ninety-one patients (1 year=78), (2-7 years=42), (>7-12 years=22) were included. TRS total, targeted tremor and activities of daily living (ADL) scores were significantly improved compared to pre-surgery up to 12 years. PDQ-39 ADL, emotional wellbeing, stigma, and total scores were significantly improved up to 7 years after surgery. At the longest follow-up, only the PDQ-39 stigma score was significantly improved and PDQ-39 mobility significantly worsened.

Discussion: This study represents the largest sample size with the longest follow-up evaluation of QoL after unilateral DBS for ET. Further studies should examine QoL using an ET-specific assessment.

Conclusions: TRS tremor and ADL scores were significantly reduced for up to 12 years after unilateral VIM DBS. The stigma component of QoL as measured by the PDQ-39 was significantly improved up to 12 years after surgery. Although other domains of QoL were improved up to 7 years compared to pre-surgery, these benefits did not remain significant at the longest up to 12-year follow-up, likely related in part to changes due to aging and co-morbidities.

Movement disorders

Resting state fMRI reveals functional networks implicated in impulsivity in Parkinson's disease

Won Kim

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Introduction: The subthalamic nucleus (STN) is a common target for deep brain stimulation (DBS) in patients with Parkinson's disease (PD). However, the associated neurocognitive sequelae include the increased risk of impulsivity and impulse control disorders (ICDs). Using magnetic resonance imaging to evaluate functional and structural connectivity via resting state fMRI and diffusion tractography imaging (DTI), respectively, we investigated differences between PD patients and age-matched controls in the hyperdirect network interconnecting the STN, orbitofrontal cortex (OFC), and primary motor cortices (PMC).

Methods: Eight PD patients and 16 age-matched, healthy controls with resting state fMRI were analyzed using FSL. Functional connectivity was evaluated at the group level, using bilateral STN and hand PMC as seeds (cluster $z > 2.3$, $p < 0.05$). Diffusion tractography was assessed on a patient-by-patient basis.

Results: In PD patients, PMC-rOFC (right orbitofrontal cortex) functional connectivity was decreased relative to age-matched controls. MR tractography revealed direct structural connectivity between STN and PMC in all patients and right STN and rOFC in 75% of patients.

Discussion: As decreased OFC activity has been associated with greater impulsivity, these findings highlight a potential functional and structural pathophysiological substrate for the increased incidence of ICDs in PD patients. Moreover, the connectivity between the right STN and OFC may account for the commonly observed complication of impulsivity following STN DBS.

Conclusion: Diffusion tractography and resting state fMRI can be used to give insight into STN-OFC networks that may contribute to increased impulsivity in PD patients at baseline and following STN DBS.

Movement disorders

Anatomophysiological Definition of the Posterior Subthalamic area for the Treatment of Parkinson's D

FRANCISCO VELASCO M.D.

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Introduction: Electrical Stimulation of posterior subthalamic area (PSA) has been reported superior to SNT in controlling Parkinson's disease (PD) symptoms.

Objective: To define the optimum target for PD control by their electrophysiologic characteristics (microelectrode recordings, evoked potentials and microstimulation) in a group of 21 electrodes inducing over 80% improvement in UPDRS of contralateral extremities in a follow up from 24 to 48 months. Defining the stimulated volume with MRI using DTI sequence with 3T/120 directions. The effect of stimulation of PSA on cortical, subcortical and brain stem structures was studied by PET-CT using 18 FDG as marker, before and after efficient electrical stimulation.

Results: A critical volume of 4.7 x 3.6 x 2.8 mm was defined by the contacts used for bipolar stimulation in patients with excellent control in PD symptoms. Microelectrode recordings showed that the target corresponded to fibers (not nuclei) in PSA between red nucleus, STN and caudal Zi. Tractography identified 3 main components of fibers converging in this target: one between deep cerebellar nuclei and ventral thalamus, other between Gpi and dorsal pons and a third between mesencephalic tegmentum and orbitofrontal (OF) cortex. PET-CT showed a tendency to increase metabolic activity in OF brain stem and putamen bilateral to efficient electrode stimulation of PSA.

Conclusions: PSA optimum target correspond to an area of fibers marked as prelemniscal radiation that link brain stem, thalamus, Gpi and orbitofrontal cortex and may be identified by high resolution tractography

Movement disorders

DBS of the substantia nigra pars reticulata improves forelimb akinesia in the hemi-parkinsonian rat

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Introduction: The traditional targets for DBS in PD significantly improve motor function; however, non-motor complications can temper enthusiasm for these targets in certain patients.

Methods: In this study, we assess whether stimulation of the substantia nigra pars reticulata (SNr) improves motor function and thus may be a potential novel target for DBS.

Results: Prior to SNr stimulation, hemiparkinsonian rats predominantly used their unimpaired forepaw 91.2 + 3.4% and 90.0 + 4.2% of the time in the stepping and limb-use asymmetry tests; After SNr-DBS (150Hz), they touched equally with both forepaws, similar to naïve and sham-lesioned rats. In vivo electrophysiological studies in a moving hemiparkinsonian rat revealed that SNr-DBS decreased β oscillations (12-30 Hz) in the SNr. Work in an anesthetized hemiparkinsonian rat showed that SNr-DBS decreased SNr neuronal spiking activity from 37.2 + 2.1 Hz to 14.7 + 2.5 Hz while increasing neuronal spiking activity from 10.5 + 1.9 Hz to 25.6 + 4.0 Hz in the ventromedial thalamus (VM), the primary SNr efferent target. High frequency stimulation (150 Hz) of SNr in brain slices from normal and dopamine-depleted rat pups resulted in a depolarization block.

Discussion: Taken together, we demonstrate a dramatic improvement of forelimb akinesia with SNr-DBS and suggest that this motor effect may be the result of attenuating SNr neuronal activity, decreasing β oscillations and increasing the activity of VM thalamic neurons.

Conclusion: SNr may be a plausible DBS target for treating motor symptoms of DBS. Further work is necessary to assess its impact on non-motor complications

Movement disorders

EMG-Based Predictive On-Off Controller of DBS for Parkinson and Essential Tremor Patients

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INTRODUCTION: We present initial patient results on adequacy of an algorithm for predicting tremor in Parkinson (PD) and Essential Tremor (ET), where prediction is based on EMG signals taken from patient's limbs. This algorithm is the basis for a noninvasive predictive on-off controller of Deep-brain stimulation in such patients, The prediction algorithm serves to switch on/off any train of DBS pulses, without modifying any pulse parameters of any DBS paradigm, using wireless link.

METHOD: Surface EMG was taken on forearm of six patients (3 PD, 3 ET) while short DBS pulse-trains were applied, followed by tremor-free periods without DBS. Stochastic parameters of EMG signals served to predict tremor-onset (if any) before tremor re-appeared, allowing reapplication of next DBS pulse-train for keeping patient tremor-free.

RESULTS: 191 cycles (events) of stimulation pulse-trains (15-60 sec) followed by 40-60 sec. wait periods without stimulation:
 PD: Average (3 patients): Sensitivity: 0.974, Specificity: 0.704, R1= 88% %, R2= 57.2%
 ET: Average (3 patients): Sensitivity: 1.0, Specify: 0.803, R1= 98.6%, R2= 81.3%
 R1= [total no-DBS-no-tremor predicted time]/[total no-BBS-no tremor actual time]
 R2= [total no-DBS-total DBS time]/[total DBS time]

DISCUSSION: Predictive control based on EMG alone can be effective in some PD/ET patients. R1, R2 would be higher since often no tremor occurred over waiting time, while stimulation was restarted every 40-60 seconds regardless

CONCLUSIONS: EMG-based predictive control of DBS via an add-on noninvasive controller is feasible regardless on previously implanted or future DBS patients, providing stimulation only when needed.

Movement disorders

Factors affecting early decline of executive function after STN DBS in Parkinson disease

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Introduction: Subthalamic nucleus deep brain stimulation (STN DBS) is an effective treatment for medically refractory Parkinson disease (PD). However, some patients show decline of executive function in the early period after STN DBS. Although this problem is usually transient, it may cause social maladjustment. We studied factors affecting early decline of executive function after STN-DBS.

Methods: Fifty-seven patients whose preoperative global cognitive screening was normal (MMSE score; 28 or more) were enrolled in this study. Executive function was evaluated with the Trail-Making Test (TMT) preoperatively and 1-month after surgery. We considered a patient to have decline in executive function if the TMT (B-A) was prolonged more than 30 seconds after STN DBS. Among 57 patients, 25 patients were categorized as having decline of executive function.

Results: Univariate analysis showed that a high preoperative UPDRS III motor score in the medication-off period and a depressive state evaluated with BDI-II correlated significantly with decline in executive function. Multiple logistic regression analysis revealed the depressive state and low frontal assessment battery (FAB) score to be the most probable independent variables predicting decline of executive function. Postoperative factors such as active contact location or dopaminergic medication reduction showed no relation to the decline.

Conclusions: Simple cognitive screening alone could not predict early deterioration of executive function after STN DBS. More detailed assessments of preoperative mood status and frontal lobe function are important.

Movement disorders

How Accurate is the StarFix Frameless DBS System?

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Introduction:

Deep brain stimulation (DBS) requires precise targeting within a high degree of accuracy, a condition previously met only by the use of a stereotactic frame. We evaluate the use of the STarFix microTargeting Platform system (FHC, Bowdoinham, ME), whereby a skull-mounted stage can be custom generated based on preoperative imaging and planning done in the outpatient setting, saving time in the operating room.

Methods:

Total number of patients were 194(368 leads): STN(116 patients), VIM(68 patients) and GPI(10 patients) underwent deep brain stimulation using the STarFix microTargeting Platform system between January 2007 and August 2011. Postoperative CT images were fused to preoperative CT and MR images to evaluate accuracy of DBS electrode placement using VoXim surgical planning software. Electrode deviations were calculated in the x, y and z planes and absolute distance between points.

Results:

The deviation of the final lead placement from the planned target using the StarFix microTargeting Platform system without accounting for brain shift was: $x=1.1$ mm(± 0.8); $y=1.5$ mm(± 1.1), and $z=1.7$ mm(± 1.2), with an overall distance of 2.9 mm(± 1.3).

Discussion:

Our results compare favorably to the targeting accuracies described in the literature using frame-based techniques. The largest deviation in our data is in the z axis, which is influenced most by neurophysiologic monitoring.

Conclusions:

Electrode placement in small targets using FHC microTargeting platform has a high accuracy. This is comparable to reported accuracy of frame based stereotactic targeting.

Movement disorders

Long-term Recordings of Local Field Potentials from Implanted DBS Electrodes for Parkinson's Disease

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Introduction: Deep brain stimulation (DBS) of the subthalamic nucleus (STN) is an effective treatment for Parkinson's disease (PD). However, DBS is not responsive to individual patient disease state, and programming parameters, once established, do not change to reflect symptoms. Much interest has focused on using local field potentials (LFP) recorded from DBS electrodes as a biomarker for PD disease state. However, no data exist from patients about what happens to LFPs over the implant lifetime. We therefore investigated whether LFP amplitude and response to limb movement differed between patients implanted acutely with STN DBS electrodes vs patients implanted 2-7 years prior.

Methods: We recorded LFPs at DBS surgery time (9 subjects), 3 weeks following initial placement (9 subjects), and 2-7 years (median: 3.5) later during implanted programmable generator (IPG) replacement (11 sides). LFP power-frequency spectra for each of 3 bipolar electrode derivations of adjacent contacts were calculated over 5-minute resting and 30-second movement epochs. Monopolar impedance data were used to evaluate trends over time.

Results: There was no significant difference in $\hat{\beta}^2$ -band LFP amplitude between initial OR and 3-week post-OR recordings ($p=0.94$). However, $\hat{\beta}^2$ -band amplitude was lower at IPG replacement time than in OR ($p=0.008$) and post-OR recordings ($p=0.039$). Impedance measurements declined over time ($p<0.0001$).

Discussion: Postoperative LFP activity can be recorded years after DBS implantation, and demonstrates a similar profile in response to movement as during acute recordings.

Conclusion: These results support the feasibility of constructing a closed-loop, patient responsive DBS device based on LFP activity.

Movement disorders

Optimizing computational feature sets for subthalamic nucleus localization in DBS surgery

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Introduction

Microelectrode recording is an adjunctive method for functional localization of the subthalamic nucleus (STN) during deep brain stimulation (DBS). Attempts to automate the process have produced numerous quantitative features extracted from these recordings. The goal of this study was to evaluate the impact of these features in the context of a multi-feature algorithm currently utilized to help distinguish the STN during DBS surgery.

Methods

We performed forwards and backwards feature selection to select the optimal feature set from thirteen previously reported features using the following supervised learning classifiers: Logistic Regression, Gaussian Naïve Bayes, K-Nearest Neighbors, and Support Vector Machines. We calculated classification error from data collected from 28 patients using a hold-one-patient-out validation scheme. Additionally, we compared the effects of pooled-normalization and self-normalization schemes on classifier performance.

Results

Optimum feature sets included five to seven features out of thirteen. Feature selection and self-normalization provide superior performance compared to non-optimized, pooled-normal classifiers. Relative error reduction for feature-optimized classifiers were 2.18% ($p=0.0137$), 12.48% ($p=0.0012$), 2.33% ($p=0.1581$), and 2.83% ($p=0.0146$), for LR, GNB, KNN, and SVM, respectively. Incorporating self-normalization with feature selection resulted in relative error reductions of 35.66% ($p=0.0018$), 35.51% ($p=0.0009$), 41.91% ($p<0.0001$), and 42.59% ($p<0.0001$), respectively.

Discussion

Feature selection significantly reduces classification error by pruning unhelpful features. Additionally, marked improvement seen with self-normalization suggests variability in neurophysiology that requires patient-specific approaches for clinically reliable automation.

Conclusion

Feature selection with patient self-normalization significantly increases accuracy in localizing the STN during DBS surgery.

Movement disorders

Simultaneous detection of oxygen and dopamine by carbon nanofiber using fast scan cyclic voltammetry

Dr. Jessica Koehne

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Introduction: Deep brain stimulation (DBS) is a state-of-the-art neurosurgical treatment for patients with movement and psychiatric disorders. While the mechanism remains poorly understood, previous studies have shown that DBS evokes release of neurochemicals and induces activation of fMRI blood oxygen level-dependent (BOLD) signal in distinct areas of the brain, including the basal ganglia network. In this study, carbon nanofiber (CNF) electrodes were integrated with the Wireless Instantaneous Neurotransmitter Concentration Sensor (WINCS) system to detect mixtures of dopamine (DA) and oxygen (O₂) using fast scan cyclic voltammetry (FSCV).

Methods: The WINCS system was combined with a 3x3 multiplexed electrochemical sensor, utilizing CNFs as electrodes, to simultaneously detect O₂ and DA at various concentrations in vitro. The sensitivity and crosstalk was evaluated at the CNF electrode during the application of simultaneous interleaved waveforms.

Results: Results demonstrate that different waveforms can be applied simultaneously to adjacent electrode pads with minimal crosstalk and with sensitivity comparable to that of the carbon fiber microelectrode. Multichannel recording can help improve detection selectivity through the application of optimized waveforms for each particular analyte.

Discussion: In conjunction with the ability to apply different waveforms for detection of multiple neurotransmitters, the CNF array has the capability of providing increased spatial resolution for neurochemical detection, which may improve our understanding of the pathophysiology of these disorders of the nervous system and the mechanism of DBS.

Conclusion: Future combination of DBS and multiplexed FSCV may lay the foundation for development of an implantable "smart" DBS system that utilizes neurochemical feedback control.

Movement disorders

The right ventral subthalamic nucleus is involved in emotional processing

Zvi Israel

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Introduction

Emotional and behavioral changes following deep brain stimulation (DBS) are observed in Parkinson's disease (PD) patients and support a possible limbic function of the subthalamic nucleus (STN).

Methods

To explore the purported limbic role of the STN, 11 PD patients undergoing DBS surgery were exposed to emotive voices during microelectrode recording (MER) of 18 STN trajectories.

Results

The right ventro-medial non-oscillatory region (VMNR) of the STN was associated with larger responses to emotive stimulation in comparison to the left VMNR and to the dorso-lateral oscillatory regions (DLOR) of the STN.

Discussion

It is proposed that DBS of the left DLOR might be associated with minimal psychiatric side effects in this patient group. The right VMNR should be further studied as it may be related to emotional symptoms of PD including depression and anxiety. Adjusting right sided STN stimulation parameters may relieve psychiatric side effects of STN DBS.

Movement disorders

Validating diffusion tensor imaging of the thalamus with intraoperative microelectrode recording

Hiroki Toda

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Introduction: Identification of the anteroposterior borders of the ventral thalamic nuclei is important in thalamic stimulation surgery. We have reviewed magnetic resonance imaging data in three patients with tremor who underwent thalamic stimulation.

Methods: We have analyzed the radiographical boundaries of the thalamic ventral nuclei using a deterministic and a probabilistic tractography algorithms with 3-Tesla diffusion imaging data. These tractography results are reviewed with structural magnetic resonance images and intraoperative microelectrode recording data of the thalamic ventral nuclei.

Results: The length of the motor-somatosensory boundaries was 5.5 to 8.5 mm. The highest connectivity of hand motor area was located at 12 to 16 mm lateral from the midline and 6 to 10mm anterior to the posterior commissure on the anterior and posterior commissural plane. The distance from the pyramidal tract to the implanted electrode was 1.8 to 3.3 mm.

Conclusion: Diffusion tensor imaging is useful for preoperative estimation of anteroposterior border of the thalamic ventral nuclei, which support safe and effective surgical planning of the thalamic stimulation.

Movement disorders

Subthalamic nucleus (STN) DBS in DYT1 dystonia

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Introduction

DYT1 dystonia can be improved with GPi DBS, but it is unknown if other brain targets could also be effective. As part of our ongoing study of STN DBS in primary dystonia(1), we enrolled three subjects with DYT1 dystonia.

Methods

Subjects were implanted in the motor territory of the STN with Medtronic model 3389 leads (two subjects bilaterally, one subject unilaterally), and followed by a movement disorders neurologist.

Results

Subject 1-(16/M) had bilateral upper extremity, cervical, and truncal dystonia with associated dystonic arm tremor and experienced complete resolution of dystonia by 6-months post-op with sustained benefit (18-months). Subject 2-(51/F) had L>R upper extremity dystonia and associated tremor who after unilateral right STN DBS had substantial improvement in tremor with some improvement in proximal dystonia (18-months). Subject 3-(46/M) had severe dystonic head tremor and left upper extremity tremor with writerâ€™s cramp who after surgery had dramatic improvement in dystonic head tremor and some improvement in left arm dystonia (3-months). All subjects experienced transient dyskinesia while optimizing stimulation parameters.

Discussion

To our knowledge, this is the first report of STN DBS for the treatment of DYT1 dystonia. The effectiveness of STN DBS in this cohort needs to be confirmed in a larger group.

Conclusion

As has been previously shown for Parkinsonâ€™s disease, it is likely that symptom improvement in DYT1 dystonia can be achieved by DBS at multiple points in the basal ganglia-thalamocortical circuit.

(1) Ostrem J, et al. Subthalamic nucleus deep brain stimulation in primary cervical dystonia. *Neurology* 2011;76(10):870-878.

Movement disorders

Does switching DBS patients from constant voltage to constant current stimulation, alters DBS stimul

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Sauzzane Sinclair (none)

Introduction: DBS has an established role to ameliorate symptoms of movement disorders, and is gaining acceptance in treatment resistant major depression, obsessive compulsive disorders, and epilepsy. For decades DBS was reliant on constant voltage (CV) for stimulation. This study evaluated the consequences of switching patients from CV to CC.

Methods: Forty implanted DBS leads in 21 patients; 24STN, 4Gpi, and 12Vim for 12PD, 7ET and 2DY. Ten were males and 11 females with mean age of 61 years (SD24). To switch patients from CV to CC, a pocket adaptor was used. We have recorded the CV-IPGs amplitude, PW, frequency and impedance of each of the 40 leads six months prior to the planned switch over. After switch over, the active contacts were not altered, and once patients and programmer were satisfied that a steady state of stimulation using the CC-IPGs was reached and had achieved similar or better control of the symptoms compared to their control preswitch-over, the IPGs were interrogated and their parameters were recorded and compared to preswitch-over.

Results: The main difference between stimulation parameters before and after the switch-over were decreased amplitude ($p < 0.001$) and increased impedance ($p < 0.05$). because the programmers aimed to retain the active and positive contacts, frequency and pulse width of the stimulation at the same settings before and after the switch over from CV to CC.

Conclusion: This study demonstrated switching DBS from constant voltage to constant current significantly reduces the amplitude, increases the impedance with insignificant decrease in pulse width and frequency.

Movement disorders

Optimal Guide Cannula Length for Transventricular Trajectories During STN Deep Brain Stimulation

David McMullen

David McMullen (none), Eric Hargreaves, PhD (none), Shabbar Danish, MD (none)

Introduction: Deep brain stimulation (DBS) trajectories targeting the subthalamic nucleus (STN) are typically planned to avoid the lateral ventricle. However, patient cortical anatomy sometimes necessitates a transventricular trajectory. Guide cannulae that do not penetrate the inferior ependymal wall can result in stimulating lead deflection. This project quantifies the minimal guide cannula above target length (ATL) to ensure complete traversal of the ventricle during DBS surgery.

Methods: A retrospective analysis of 50 trajectories in 26 patients was conducted. Trajectories anchored to the STN target-location were rotated medially, thereby decreasing the azimuth while keeping the declination fixed. A maximal 5.5° rotation was allowed, that was based on a 14-mm burr hole diameter and a mean 77mm coronal suture to STN distance. ATL from the inferior ependymal wall to STN was noted for modified trajectories with ventricular involvement.

Results: Ventricular involvement was identified in 11/50 modified trajectories. The mean ATL was 29.33mm (SEM=0.41; range=26.4-31.3mm) with 8 trajectories less than 30mm and none less than 25mm ATL ($p=0.0058$).

Discussion: Transventricular trajectories for DBS are sometimes unavoidable. In these instances, ensuring that a guide cannula traverses the entire ventricle and pierces the inferior ependymal wall may minimize stimulating lead displacement. Determining the standard ATL cannula length that will allow neurosurgeons to minimize complications with only a minor modification in their surgical procedure.

Conclusions: Our results show that whereas a standard 30-mm ATL cannula does not prevent the possibility of lead deflection during transventricular trajectories, using a 25mm ATL cannula will prevent this outcome.

Movement disorders

Clinical outcomes in a series of X-linked Dystonia Parkinsonism treated with bilateral pallidal DBS

Camilla Kilbane, MD

(Industry Grant Support, Company: Medtronic Educational Fellowship Grant)

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Introduction:

X-linked dystonia parkinsonism (DYT3/Lubag disease) causes adult onset progressive dystonia & parkinsonism which may not respond to pharmacotherapy. Four isolated case reports have shown beneficial effect with GPi DBS. Here we present the clinical outcome in a case series of DYT3 positive patients treated with bilateral GPi DBS at our center.

Methods:

Three male patients (32, 44, 65 years old) were treated with bilateral GPi DBS. All patients presented with medication refractory generalized dystonia with prominent cranial/axial features and some parkinsonism. Clinical outcomes were measured at baseline as well as post-operatively using blinded rater Burke-Fahn-Marsden Dystonia rating scale (BFMDRS) at various time points.

Results:

Mean percentage improvement in BFMDRS was 70 %, (range 36 – 96%) at the last follow up (average 6 months). Interestingly 2 patients developed transient worsening of gait while optimizing DBS settings resulting in shuffling and freezing of gait. These symptoms resolved by reducing the frequency or removing the lowest contact of stimulation.

Discussion:

Bilateral GPi DBS offered significant symptomatic benefit in all patients. Transient worsening in parkinsonian gait symptoms was present in two patients but resolved with programming efforts. This therapy should be considered in cases of severe refractory Lubag dystonia.

Conclusion:

Bilateral pallidal DBS offered significant improvement in dystonic symptoms, however long term follow up is needed. The benefit seen in lubag's dystonia is more favorable than in secondary dystonia syndromes.

Movement disorders

Clinical outcomes & neurophysiological findings in Holmes tremor patients treated with Pallidal DBS

Camilla Kilbane, MD

(Industry Grant Support, Company: Medtronic Educational Fellowship Grant)

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Introduction:

Holmes tremor (HT) is characterized by irregular, low frequency (<4.5 Hz) tremor occurring at rest, posture and action, often affecting proximal muscles. We report the outcome and neurophysiological finding for HT treated with Globus pallidus interna (GPi) Deep Brain Stimulation (DBS).

Methods:

4 patients were treated with unilateral GPi DBS for management of intractable HT. Clinical outcomes were measured at baseline and after surgery using an abbreviated motor severity Fahn-Tolosa-Marin Tremor rating scale (FTMTRS). Intra-operative microelectrode recordings (MERs) were performed in the awake state. MERs were spike sorted off-line and analyzed for firing rate and oscillatory activity.

Results:

Mean percentage improvement in tremor motor severity was 76.5% (range 58-90%). Average length of follow up was 33.7 mos (range 18-52). 27 neurons were recorded in the resting state and 12 of these were also recorded during contralateral voluntary arm movement. The mean firing rate at rest was 56.11 (+/-28.5) and 63.56 (+/-19.4) with action. The percentage of cells with 2-5 Hz oscillations was significantly higher than for a comparison group of GPi recordings in PD.

Discussion:

GPi DBS provided excellent symptomatic tremor control in our cohort. The mean neuronal firing rate was lower in HT patients than what has previously been reported in Parkinson's disease. The finding of extensive GPi neuronal oscillatory activity at tremor frequency in HT provides a physiological rationale for target selection in this disorder.

Conclusion:

GPi DBS provided excellent tremor control in our cohort of patients.

Movement disorders

Clinical outcomes of deep brain stimulation patients as a function of angle of target approach

James McInerney

Elana Farace (none), Joshua Stone (none)

Deep Brain Stimulation (DBS) is an established treatment for Parkinson's Disease (PD). There is little data addressing whether the angle of approach to the stimulation target has any effect on outcomes. We assessed the clinical outcomes of DBS patients as related to the angle of approach.

We conducted a quality assurance review of our DBS database to identify patients treated for PD with DBS targeting the subthalamic nucleus (STN) and with postoperative outcomes available for review. Angles employed operatively were compared with clinical outcomes. Primary outcome measures were neuropsychological evaluation with Dementia Rating Scale (DRS) and Mini-Mental Status Exam (MMSE), change in medication requirement and patient-reported symptom change at 3, 6 and 12 months.

One hundred patients fit criteria. Anterior approach angle range was 7-34.6 (mean 24) and lateral angle range was 3-36.3 (mean 18). Angles in the range of 20-30 anterior and 12-18 lateral were considered in range and all others out of range. At 6 months, patients out of range anteriorly had significantly lower MMSE scores than patients in range ($F=3.9$, $p=.015$), and at one year had significantly lower DRS scores ($F=3.57$, $p=.044$). At 3 months, patients out of range laterally showed significantly worse outcomes in symptoms ($F=26.5$, $p=.001$), medication changes ($F=3.6$, $p=.05$) and MMSE scores ($F=3.2$, $p=.05$) than patients in range, though, these differences resolved later.

These findings suggest that attention should be paid to the angle of approach when planning DBS cases. Approach angles out of normal range may have a negative impact on outcome.

Movement disorders

Development of wireless DBS technology combining electrochemical sensing and neurostimulation: Mayo

Aimen Kasasbeh

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Introduction

Previously, we developed a neurochemical monitoring device called WINCS (Wireless Instantaneous Neurochemical Concentration Sensing) system, and confirmed its functionality for fast scan cyclic voltammetry (FSCV) monitoring during human DBS neurosurgery. Because the electrical pulses produced stimulus artifacts in the FSCV recordings, identifying the precise neurochemical(s) released during DBS was problematic. To resolve this and to initiate feedback-control capability, we developed a novel stimulation device called Mayo Investigational Neuromodulation Control System (MINCS), which provides wirelessly controlled stimulation interleaved with FSCV.

Methods

The MINCS design incorporated analog circuitry for current and voltage isolated electrical stimulation, a microprocessor, a Bluetooth transceiver, a single battery-powered, multilayered printed circuit board, and coupling to WINCS with an optical connection. In vivo testing of MINCS was performed in the anaesthetized rat, where stimulation electrode was placed in the medial forebrain bundle (MFB), and WINCS FSCV recordings were obtained in the striatum.

Results

MINCS evoked dopamine release detectable by WINCS at the striatum, as measured by simultaneous and interleaved FSCV. Importantly, the controlled release of dopamine was detected without stimulation artifact during the application of variable and wirelessly controlled high-frequency stimulation,

Discussion

MINCS successfully coupled to WINCS to provide wirelessly controlled, user-designed, arbitrary waveform electrical stimulation that interleaved with FSCV scans. Allowing such ongoing monitoring of neurochemical changes during the stimulation period may pave the way towards future closed loop DBS systems.

Conclusion

Ultimately, we envision a novel DBS system of an implantable closed-loop, "smart" device incorporating a WINCS-based chemical micro-sensor, feedback control, and MINCS-based neuromodulation to maintain neurochemicals at optimal levels.

Movement disorders

Finding the Sweet Spot: Optimal DBS Stimulation in the Region of the Subthalamic Nucleus

Parag Patil

Erin C. Conrad (none), Karen S. Cummings (none), Kelvin L. Chou (none), Parag G. Patil (none), Susan V. Grube (none)

Introduction: The optimal therapeutic location of subthalamic nucleus deep brain stimulation (STN DBS) for PD remains uncertain. The goal of this study was to calculate optimal DBS lead location precisely from clinical outcome data, utilizing a validated MR sequence and neuronal-activation based, electrical field modeling.

Methods: Fifteen patients (30 leads total) underwent STN DBS surgery for Levodopa-responsive PD. High-resolution post-operative CT was co-registered to a validated pre-operative MRI visualizing the STN. Voltage information was utilized to model the electrical field and neuronal activation around each contact. Points within 5 mm of the STN midpoint were rated according to the probability of activation by neighboring leads and UPDRS improvement with and without stimulation, at 6-month follow up.

Results: The ideal lead position calculated with the model was 0.09 mm lateral, 0.86 mm posterior, and 2.22 mm dorsal to the anatomic and electrophysiological center of the STN. Leads dorsal to the STN were associated with higher improvement than those within the STN.

Discussion: Allowing simultaneous high-resolution visualization of the STN and individual DBS electrode contacts in combination with potential field modelling, our study strongly suggests that the locus of optimal stimulation lies dorsal to the STN and not within the STN. Our study agrees with previous indirect studies of optimal contact location indicating that optimal stimulation occurs just posterior and dorsolateral to the midpoint of the STN.

Conclusions: The ideal location for DBS stimulation in PD appears to be in the caudal zona incerta, dorsal to the posterolateral STN.

Movement disorders

Non-Rigid Registration for Targeting of Subthalamic Nucleus in DBS for Parkinson's Disease

Dennis M. Campbell, MD

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INTRODUCTION

STN is the DBS target of choice for medically refractory PD. Traditionally, standard stereotactic coordinates are used for targeting. We hypothesize that non-rigid registration will enable more accurate targeting of STN.

METHODS

DBS leads were extracted from post-operative scans and the position of each contact was determined. Post-operative scans were registered to the pre-operative MRI and non-linearly normalized to the atlas space. Positions of the contacts were projected from individual patient spaces onto the atlas space. A probability function was associated with each post-operative programming stimulation exam producing reduction in symptoms. These were combined to produce a map of efficacy in 3-dimensional space which was compared to a map built using each patient's stereotactic coordinates.

RESULTS

The centroid of efficacious maps built using rigid registration (11.43 lateral, -3.08 anterior, -3.18 superior) was closer to known standard targeting coordinates than the centroid of the non-rigid based maps (13.69, -0.05, -3.7). Overlaying them on the atlas MRI showed that the map built using stereotactic mapping was asymmetric and not located in the anatomical region expected to produce efficacy. Non-rigid registration produces maps located in the expected anatomical region.

DISCUSSION

In this proof-of-concept analysis, it is evident that normalizing patient data to an atlas using non-linear methods improves localization of STN. The data after non-rigid normalization is better able to account for anatomic variability among patients and the statistical maps are in a more acceptable anatomic location.

CONCLUSIONS

Non-rigid registration of data points in the planning of STN DBS provides a more accurate method for lead placement.

Movement disorders

Outcomes of Deep Brain Stimulation Treatment for Tremor Patients with Multiple Sclerosis

James McInerney

Elana Farace (none)

Deep Brain Stimulation (DBS) is an established treatment for Essential Tremor (ET). There is relatively little data addressing the role of stimulation in tremor associated with Multiple Sclerosis (MS). We assessed the clinical outcomes of MS patients treated with DBS for their tremors.

We conducted a quality assurance review of our DBS database to identify patients treated for tremors with DBS targeting the ventral Intermediate nucleus (ViM) who also had MS and with postoperative outcomes available for review. Primary outcome measures were neuropsychological evaluation with Dementia Rating Scale (DRS), Mini-Mental Status Exam (MMSE) and Hopkins Verbal Learning Test (HVLT) as well as patient-reported symptom change at 3,6 and 12 months.

We identified six patients implanted for tremor who also had MS. All patients reported improved symptoms at three months. Symptom control varied over time, but all patients remained improved with stimulation on compared to stimulation off. Neurocognitive outcomes were stable at three months with one patient showing decline in the HVLT, two remaining at baseline and the other three improved. At 12 months five of six patients did show signs of cognitive decline, which was expected with the progression of their MS.

These findings suggest that DBS is safe and effective in tremor patients who also have MS. Patients demonstrate significant short term improvement which is largely maintained over time. These patients also show only minimal short term cognitive effects, while longer term declines appear to be in keeping with their expected disease progression.

Movement disorders

Subthalamic Nucleus Upper Border Location: Microelectrode Recording and Supramammillary Commissure B

Faisal Al Otaibi

Amal Mokeem, MD (none), Thamer Al Khairallah, MD (none)

Introduction: Several internal landmarks to target subthalamic nucleus (STN) have been used in practice. This study was conducted to identify the relationship between the SMC upper border and the upper border of STN.

Methods: Six consecutive patients underwent 12 STN deep brain stimulation (DBS) for Parkinson's disease were analyzed. Red nucleus and anterior commissure - posterior commissure (AC-PC) distance based targeting methods were used to target STN. The co-ordinates (X, Y and Z) for the STN and SMC upper border were calculated. The X, Y and Z co-ordinates of the upper border of STN identified during microelectrode recording (MER) were recorded. The active DBS electrode contact co-ordinates were calculated based on fusion of postoperative CT with pre operative planning MRI.

Results: In average, SMC upper border was identified at 3.5 mms ($\hat{\pm}$ 0.6) below the mid-commissural point (MCP) whereas the top border of STN was identified at 1.9 mms ($\hat{\pm}$ 0.8) below the MCP. The average location of the STN upper border was located 1.5 mms ($\hat{\pm}$ 0.7) above the top of SMC. Average X, Y, Z co-ordinates for the location of the center of DBS electrode active contact were 11.8, - 2, and -1.7 from the MCP.

Discussions: Utilizing SMC as an internal landmark might identify the upper border of the STN. However, the small number of patients, in addition to other factors like image fusion error, and brain shift limits this study.

Conclusion: SMC might be used as an internal landmark for indirect identification of the upper STN border location.

Movement disorders

The clinical impact of precise electrode positioning in STN DBS on three-year outcomes.

Sun Ha Paek

Background: Few studies have analyzed the clinical impact of subthalamic nucleus (STN) deep brain stimulation (DBS) as a function of inserted electrode positioning.

Methods: Forty-one advanced PD patients were followed up over three years following bilateral STN DBS. Patients were evaluated using the Unified Parkinson's Disease Rating Scale (UPDRS), Hoehn and Yahr staging, Schwab and England Activities of Daily Living (ADL), and the Short Form-36 Health Survey (SF-36) before surgery and one, two, and three years after surgery. The patients were divided into two groups according to electrode position based on the fused preoperative MRI and postoperative CT images: group I included patients who had both electrodes in the STN (n=30), whereas group II included patients who did not have both electrodes in the STN (n=11).

Results: The UPDRS, Hoehn & Yahr staging, Schwab and England ADL, and the SF-36 scores showed significant improvements with decreased L-dopa equivalent daily doses (LEDDs) in both groups as well as in the group as a whole up to three years following bilateral STN DBS. However, the off-medication UPDRS total and motor (part III) scores significantly deteriorated with increased LEDDs for patients in group II three years after STN DBS in comparison to those of patients in group I.

Conclusions: We conclude that the better electrode positioning leads to the better long-term outcomes in advanced PD patients following STN DBS.

Movement disorders

Value of multi-center collaboration towards building more complete electrophysiological atlases

Benoit M. Dawant

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Introduction: Electrophysiological maps built using stimulation response data from a population of patients can be used to refine targeting in DBS. For the first time we are now able to report the value of combining data from more than one institution to create more comprehensive maps using CRAVEâ„¢ software and algorithms developed at Vanderbilt University (VU).

Method: Under an IRB data sharing protocol, we combined intra-operative high frequency stimulation response data from Parkinsonâ€™s patients undergoing STN-DBS at VU and Ohio State University (OSU). From 141 implantations at VU, we populated 595 data points causing symptoms reduction by at least 50%. From 26 implantations at OSU, we populated 270 data points causing muscular contraction. By 3D non-rigid registration between patient MRIs and an atlas MRI probabilistic maps of efficacy and contraction were built in the atlas.

Results: The efficacy map was primarily located in the dorso-lateral region of the STN while the contraction map was located within the internal capsule or at its border. These maps are complementary to each other and correlate the anatomy with the intraoperative stimulation data observed by the surgical teams.

Discussion: VU and OSU emphasize and record different aspects of physiological stimulation. Such complementary maps can be highly valuable pre-, intra- and post-operatively.

Conclusion: Combing data from multiple institutions onto a single normalized atlas demonstrates for the first time, the ability to bring complementary datasets together into a de-identified, normalized physiological atlas. The resulting maps provide more information than would be obtained using single-site maps.

Movement disorders

Current based DBS in STN for PD Achieves Asymptotic Impedance Levels Earlier than Voltage based DBS

Dr. Shabbar F. Danish

David McMullen (none), Eric L. Hargreaves (none), Rocco J. DiPaola (none), Shabbar F. Danish (none), Stephen Wong (none)

Introduction: Deep Brain Stimulation (DBS) of the subthalamic nucleus (STN) is an adjunct surgical therapy for Parkinson's Disease (PD). Subsequent post-operative programming of DBS can be performed in current or voltage modes. Programming in current mode has been suggested to be more efficient for achieving optimal/stable stimulation earlier than voltage programming by better compensating for early fluctuations in impedance.

Methods: The bipolar impedances of adjacent stimulating lead contacts of 11 bilaterally STN implanted PD patients were followed out for a mean 427 days (range 164-783). Patients were solely programmed in current or voltage modes. Individual exponential decay curves were fit to the impedance data of each stimulating lead from which the exponential decay constant τ and half-life $t_{1/2}$ parameters were derived.

Results: Analysis of the exponential decay constant indicated a trend towards significance $t(20)=1.95$; $p=0.065$ favoring the current mode with larger values, while analysis of the half life parameter revealed a significant difference $t(20)=2.56$; $p=0.018$ favoring the current programming mode with a shorter half life (30.91days) then the voltage programming mode (2229.56 days).

Discussion: The drastic difference in half lives of the decay curves can largely be attributed to 50% of the curves in the voltage programming group being better characterized as linear in nature.

Conclusion: Bipolar adjacent stimulating lead impedances achieve asymptotic levels earlier under current programming mode then under voltage programming mode. Whether this is supported by differences in clinical outcomes is under investigation.

Movement disorders

Intrathecal clonidine pump as a treatment for spasticity in multiple sclerosis: a case study.

Sylvine Cottin

François Mathieu (none), Luc Cantin (none), Michel Prud'Homme (none)

Introduction : Spasticity refractory to oral medication is a major complication of several neurological diseases and trauma including multiple sclerosis (MS). Intrathecal (IT) infusion of baclofen is one of the usual alternative, mainly for non-ambulant patients. Another alternative could be the use of clonidine, a noradrenalin agonist that has been shown to help recovery of locomotor function in animals. Intrathecal clonidine has been tested in humans for the relief of spasticity and for walking rehabilitation purposes, but has never been delivered via an infusion pump for that purpose.

Methods: Here, we present the case study of a 50 year old patient who has been suffering from MS for 20 years. She was able to walk for short distances but her ambulatory function was substantially affected because of spasticity in the lower limbs. As revealed by various walking tests and cinematic parameters, her walking pattern was severely modified by spasticity.

Results: After a successful IT bolus infusion test trial and implantation of an intrathecal clonidine pump, her spasticity decreased significantly and his ambulatory function improved after 4 months. Improvements were also identified on balance as measure on a balance platform and on her walking pattern studied with the GAITRite® system.

Discussion and conclusion: These encouraging results suggest that clonidine could be a promising alternative in the treatment of spasticity for ambulant patients. More comparative studies are however needed in order to thoroughly assess the beneficial effects of this therapy.

Movement disorders

Subthalamic Nucleus Deep Brain Stimulation Optimal Target: Meta-Analysis and Systematic Review

Shafik N. Wassef

D. Louis Collins, PhD (none), Pierre Jannin, HDR (none), Shafik N. Wassef, MD (none)

ABSTRACT:

Background: Deep brain stimulation of the subthalamic nucleus is a therapeutic option for improving motor symptoms in advanced and medication-refractory Parkinson's disease. The exact target for stimulation, however, is still uncertain and not well defined in the biomedical literature.

Objective: To localize the optimal targets for deep brain stimulation of the subthalamic nucleus in Parkinson's disease.

Methods: Systematic review and meta-analysis of the stimulation targets identified or reported in the biomedical literature. The total number of subjects includes 1190 patients who underwent STN DBS for Parkinson's disease.

Results: We report mean values for x, y, and z coordinates expressed in the Schaltenbrand-Wahren Atlas coordinate system as the best stimulation target location (x = 11.98, y = 2.63, z = 3.36).

Conclusion: The target identified in our study was within the subthalamic nucleus. The lack of standardized reporting of clinical scores made it impossible to calculate statistical correlations between three-dimensional coordinates and clinical scores. More rigorous reporting is suggested for further analysis and to provide evidence-based recommendations for an optimal stimulation site.

Movement disorders

Intraoperative VIM DBS spatial summation effects along horizontal axis in ET patients

Chris Kao

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Introduction. DBS spatial summation effects have not been tested along the horizontal axis surrounding the target. Intraoperatively, the stimulating effect was tested one point (track) at a time, either with single-track or multi-track electrode mapping. The current study simultaneously activates more than one stimulating electrode at the target and in the surrounding areas.

Methods. 3 Grass S88 Dural channel stimulators are capable of outputting up to 6 ch simultaneously via stimulating isolators. The connections were organized using a 5-ch interfacing box (Medtronic) and the output voltage and current was monitored real time by viewing the square waves using a digital scope. The effects were tested in ET patients targeting VIM using semi-macro electrodes (1x0.41 mm, IOPXXXX9CK1, FHC Inc.), and the evaluations were done by an accelerometer and a neurologist in the OR.

Results. Once the most effective track from 4 simultaneous electrodes (2 mm apart) was identified at a desired depth, 2nd and 3rd stimulations were added simultaneously. A much lower intensity (46.5% of control, n=8), 2.25 ± 1.03 Volts vs. 4.84 ± 1.56 Volts (average \pm SDV) was needed to produce the same efficacy as that single electrode when 2 electrodes (3 in some) were activated simultaneously.

Conclusion. Simultaneously activating 2 electrodes across a 2mm space significantly lowers the required voltage, producing the same efficacy. Such a spatial summation would use the minimum current to activate a bigger target tissue with fewer side effects with select particular electrodes. This has implications for future electrode design such as multi-contact directional selective electrode.

Movement disorders

Investigation of DBS Mechanisms During IPG Replacement Surgery

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Introduction: We developed an innovative paradigm for investigation of therapeutic mechanisms of deep brain stimulation (DBS) on movement disorders. Direct, temporary connection to the DBS lead during implanted pulse generator (IPG) replacement was used to study the effects of novel temporal patterns of stimulation on motor symptoms.

Methods: Patients enrolled in the IRB-approved study underwent IPG replacement using local (monitored) anesthesia. Following device explant, the DBS lead extension was temporarily connected to an extracorporeal isolated electrical stimulator using a sterile adapter cable. Different temporal patterns of stimulation were delivered while quantifying upper-extremity tremor (tri-axial accelerometry) or bradykinesia (finger-tapping). Upon experiment completion the adapter cable was disconnected and the new IPG was implanted.

Results: Among 159 IPG replacements from 2005-2011, 56 patients participated in the research study (16 ET, 31 PD, 5 mixed ET/PD tremor, 3 MS, 1 tremor/myoclonus). Surgeries were extended by 42 ± 8.2 minutes in 37 patients completing the study. Several measures of motor symptoms were significantly dependent on stimulation pattern. No post-operative infections or complications were observed in any of the 159 patients.

Discussion: IPG replacement occurs at a time when the DBS/brain interface is stable and patients demonstrate symptom reduction with known stimulation parameters. Conducting research at this time point avoids temporary microlesion effects, fluctuating electrode impedances, as well as technical limitations of contemporary IPGs, which preclude innovative stimulation paradigms.

Conclusions: IPG replacement surgeries provide advantageous conditions to conduct translational DBS research with minimal additional risk to research subjects.

Supported by NIH R01 NS040894

Movement disorders

The influence of propofol on the microelectrode recording of STN DBS

Sun Ha Paek

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Introduction: The purpose of this paper is to document the influence of propofol on electrical signals from the microelectrode recording in STN DBS under local anesthesia.

Methods: We analyzed 8 patients with advanced Parkinson disease who had been treated with bilateral STN DBS with microelectrode recordings (MERs). The electrodes of their left sides were first performed without sedatives and then the electrodes of their right sides were followed with continuous infusion of propofol (25ug/kg/min) and fentanyl (25ng/kg/min) under local anesthesia. Their MER signals from each side were compared by using mean firing rate (MFR) analysis, single unit activity (SUA) analysis, and spike sorting analysis.

Results: There is no significant difference in the MFR and bursting pattern of the typical STN in both sides of 8 patients. We isolated a total 85 SUAs from the left side and 68 single unit activities from the right side of eight patients. There is no significant difference in the MFR of single unit activities between the left side MERs (38.4 ± 17.4 spikes/sec, range: 11.2-89.4 spikes/sec, n=85) and right side MERs (36.2 ± 17.5 spikes/sec, range: 8.5-84.2 spikes/sec, n=68).

Discussion: The continuous infusion of propofol and fentanyl does not significantly interfere the MER signals from the STN. It can be a useful method applicable for the successful bilateral STN DBS in the patients with advanced Parkinson's disease under local anesthesia with acceptable clinical outcomes.

Conclusion: We found that there was little influence of propofol on the electrical signals from the microelectrode recording in STN DBS under local anesthesia.

Movement disorders

Complications of STN DBS for Parkinson's disease - a single team 10 year experience in 242 patients

Dr Raymond Cook

(University Grants/Research Support, Company: Medtronic)

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Introduction: We report a 10 year prospective study examining the short and long term morbidity of STN DBS in one surgical unit by a single surgeon/neurologist/institution.

Methods: Complications were recorded in the patient files at the time of occurrence. Chart review was undertaken for analysis.

Results: Major procedural complications were rare (1 lobar haemorrhage related to venous infarction at 48 hours (0.4%) and one perioperative seizure (0.4%). There were no deaths in this series. Six DBS leads (1.2%) were repositioned due to suboptimal positioning and six leads required replacement due to lead fracture. One further lead was replaced due to a manufacturing problem (resulting in short circuiting and rapid battery drainage). With one exception, lead complications occurred in the first thirty patients treated.

The most common problem in the postoperative phase related to mild neuropsychiatric disturbance which ranged from mood elevation to anxiety, depression and apathy. Acute psychosis requiring psychiatric admission occurred in one patient. There were a total of six infective complications (2.5%), often late after implantation with average presentation at 13.4 months (range 0.5-33 months). Infections were treated with wash out of the IPG pouch and long term antibiotics (1), total (2) or partial (3) system explantation with reinsertion (5) at 3 months - all without re-infection.

Conclusions: This relatively pure series, obtained from a single surgeon/neurologist/institution confirms at long term follow up the relative safety of STN DBS with a quantified risk relating to the procedure itself, medication reduction and long term implant infective risk usually requiring further surgery.

Movement disorders

Dexmedetomidine Utilization for Deep Brain Stimulators Implantation

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Introduction: This study was conducted to assess the effect of Dexmedetomidine (Dex) on microelectrode recording (MER), clinical features, and patients'™ comfort during deep brain stimulation (DBS) procedures.

Methods: The effects of Dex on MER and clinical features were analyzed in a subset group of 5 adult patients with movement disorders who underwent deep brain stimulation procedure. Three patients with Parkinson's™ disease underwent bilateral subthalamic nucleus (STN) DBS and two with dystonia underwent bilateral globus pallidus internus (GPI) DBS. Dex dosing was standardized according to body weight. Two to three MER tracts were used in each single target. Patients'™ comfort was measured using a simple scale of 0 to 10. The MER results and patients'™ comfort were compared to a control group of 4 patients who did not receive Dex.

Results: There was no significant effect of Dex on MER during STN or GPI DBS procedures. However, pulse artifacts were noted in most of the performed MER with the utilization of Dex (16 out of 24 MER tracts). In all Parkinson's™ disease patients, Dex reduced rigidity as compared to pre-operative assessment. The group who received Dex had an increased intraoperative comfort as compared the control.

Discussion: Dex does not have any significant effect on MER; however, it may increase pulse artifacts during MER. Dex utilization has increased patients'™ comfort during procedure.

Conclusion: Dexmedetomidine utilization in DBS procedures does not affect MER and increase intraoperative patients'™ comfort. However, it can affect intraoperative clinical assessment of stimulation related benefit.

Movement disorders

Putaminal DBS for the Treatment of Essential Tremor

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Delson J. Silva, MD, MSc (none), Isabela P. Gomes (none), Paulo C. Ragazzo, MD, PhD (none)

Introduction:

Vim-DBS is the best surgical option for the treatment of refractory essential tremor (ET). Posterior ZI and STN are the current alternative targets. It is generally assumed that ET is secondary to a dysfunction of the olivorebellothalamic system. Vilela Filho et al (2001), Kim et al (2006) and Lim et al (2010) reported one case each of ET improvement/abolishment following a contralateral posterior putamen infarct. Vilela Filho (2006) demonstrated that harmaline-induced tremor in rats was significantly reduced ipsilaterally to previously performed unilateral posterior striatotomy. Based on the aforementioned data, we have hypothesized that ET is due to the hyperactivity of the posterior putamen. We here report the case of a patient submitted to unilateral putaminal DBS in whom Vim and STN intraoperative stimulation failed to induce tremor reduction.

Methods:

A 29-year-old female patient presenting with refractory bilateral postural distal upper limb tremor and family history of ET underwent left posterodorsal putamen DBS and right Vim thalamotomy. Putamen coordinates were obtained from T2-weighted 3D axial slices: 3.0mm anterior, 3.0mm above and 27.0mm lateral to the MCP. Macrostimulation with 3.0V/100Hz produced tremor arrest without side-effects.

Results:

There were no surgical complications. Persistent tremor abolishment was achieved contralaterally to the putaminal DBS after a 1-month follow-up period. Stimulation parameters: monopolar/3.5V/130Hz/90 μ s.

Discussion/Conclusions:

Despite the short-term follow-up, we are tempted to conclude that the posterodorsal putamen may prove to be an excellent alternative target for the treatment of ET. Besides, the results obtained seem to support the hypothesis previously advanced by the authors.

Movement disorders

Subthalamic Nucleus Upper Border Location: Supramammillary Commissure-Based Method

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Introduction: Several internal landmarks to target subthalamic nucleus (STN) have been used in practice. This study was conducted to identify the relationship between the SMC upper border and the upper border of STN.

Methods: Six consecutive patients underwent 12 STN deep brain stimulation (DBS) for Parkinson's disease were analyzed. Red nucleus and anterior commissure - posterior commissure (AC-PC) distance based targeting methods were used to target STN. The co-ordinates (X, Y and Z) for the STN and SMC upper border were calculated. The X, Y and Z co-ordinates of the upper border of STN identified during microelectrode recording (MER) were recorded. The active DBS electrode contact co-ordinates were calculated based on fusion of postoperative CT with pre operative planning MRI.

Results: In average, SMC upper border was identified at 3.5 mms ($\hat{\pm}$ 0.6) below the mid-commissural point (MCP) whereas the top border of STN was identified at 1.9 mms ($\hat{\pm}$ 0.8) below the MCP. The average location of the STN upper border was located 1.5 mms ($\hat{\pm}$ 0.7) above the top of SMC. Average X, Y, Z co-ordinates for the location of the center of DBS electrode active contact were 11.8, - 2, and -1.7 from the MCP.

Discussions: Utilizing SMC as an internal landmark might identify the upper border of the STN.

Conclusion: SMC might be used as an internal landmark for indirect identification of the upper STN border location. However, the small number of patients, in addition to other factors like image fusion error, and brain shift limits this study.

Movement disorders

Bilateral Globus Pallidus Internus Deep Brain Stimulation for Woodhouse Sakati Syndrome

Faisal Al Otaibi, MD

Amal Mokeem, MD (none), Faisal Al Otaibi, MD (none), Thamer Alkhairallah, MD (none)

Introduction: Woodhouse Sakati syndrome (WSS) is a very rare autosomal recessive neuroendocrine disorder. Extrapyrmidal neurological manifestations are mainly characterized by dystonia and chorea. Here, we report two cases of WSS, who underwent bilateral globus pallidus internus deep brain stimulation (GPi DBS).

Methods: A retrospective analysis of two patients with WSS was conducted. Clinical, radiological, and biochemical features were analyzed. Both patients underwent bilateral GPi DBS. The follow-up period was 6 years for the first patient and one year for the second.

Results: The first patient was a 40 year-old male, who became bedridden due to generalized dystonia and suffered from diabetes mellitus. Magnetic resonance image (MRI) brain featured white matter abnormal signals at the centrum semiovale. Bilateral GPi DBS did not improve his dystonia. The second patient was a 19 year-old male who suffered from generalized dystonia with severe jaw dystonia limiting his oral intake. He developed weight loss secondary to jaw dystonia. MRI brain was normal. Overall, he had a good response to GPi DBS. Jaw dystonia responded more than extremities. When the device was accidentally switched "off", he developed locked jaw after 24 hours and improved over 10 hours from turning the device "on".

Discussion: WSS is a very rare syndrome that is associated with generalized dystonia. GPi DBS can improve this symptomatology. MRI abnormality may predict the response to DBS.

Conclusion: Bilateral GPi DBS can improve dystonia in WSS. However, the degree of benefit is almost similar to other secondary dystonias.

Movement disorders

Unilateral deep brain stimulation of the subthalamic nucleus for Parkinson's disease

Michael Sobstyl

Maciej Jakuciński (none), Mirosław Ziębik (none), Sebastian Dzierżewski (none), Wojciech Górecki (none)

Introduction: The aim of this study was to assess the results of unilateral deep brain stimulation (DBS) of the subthalamic nucleus (STN) for the treatment of idiopathic Parkinson's disease (PD).

Methods: The clinical series consists of 31 consecutive PD patients. The patients underwent unilateral magnetic-resonance imaging-guided STN DBS. All procedures were performed under local anesthesia. The STN was confirmed only by macrostimulation. All patients were assessed according to a modified Core Assessment Program for Intracerebral Transplantation. The patients were assessed preoperatively and at 6, 12 and 18 months after surgery. 25 patients were followed for 18 months. **Results:** Medication off/stimulation on total UPDRS motor scores were improved by 29 +/-7 % when compared to the baseline medication off motor scores. The contralateral motor scores improved by 54 %, ipsilateral motor scores by 14 %, whereas the axial motor scores by 33 % in medication off/stimulation on condition. The duration and severity of levodopa induced dyskinesia were reduced by 78 %. The daily levodopa dose was decreased by only 15 +/-10 %.

Discussion: Unilateral STN DBS may be a sufficient treatment for patients with asymmetry of PD symptoms. Patients with advanced age may gain more benefit from unilateral STN DBS than simultaneous bilateral STN DBS which can be associated with higher chance of postoperative confusion and dysarthria.

Conclusion: Unilateral STN DBS is a safe and effective procedure for selected patients with medically refractory PD motor symptoms.

Movement disorders

Case report: Successful management of hemiballism from delayed peri-STN DBS hemorrhage

Aqueel Pabaney

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Introduction: Although patients undergoing subthalamotomy for PD may develop transient hemiballism-hemichorea, this movement disorder hasnâ€™t been reported as a late complication of STN DBS.

Case: A 54 year-old male underwent placement of STN electrodes for medically-refractory PD with excellent microlesional effects bilaterally and subsequent good control of Parkinsonian symptomatology. Ten weeks later, after having restarted aspirin, a fall caused a small left-sided peri-electrode hemorrhage. He immediately developed near-continuous, contralateral hemiballismus of such violence that he had to be hospitalized due to elevated CPKs from bruising. Drugs trials (including haloperidol) were unsuccessful, except for high doses of sedatives. Involuntary movements improved somewhat from large-field, low-frequency (c+0-1-2-3-, 20Hz, 360 PW, 2.5V) stimulation through the left electrode, but not enough to permit ambulation. Two weeks later, the left STN electrode was replaced by a new left electrode in the GPi under general anesthesia. Initially there was some insertional effect. High-frequency GPi DBS (c+1-, 160Hz, 90 PW, 2.0V) abolished his hemiballism-hemichorea. The improved right limb anti-Parkinsonian effect was enhanced with levodopa.

Conclusions: Late hemorrhage around DBS electrodes is rare. The risks and benefits of antiplatelet therapy need careful evaluation in DBS patients, especially if they are prone to falls. In this case, low-frequency STN stimulation diminished the hemiballism-hemichorea somewhat, suggesting its use as a therapeutic modality for hyperkinetic movement disorders. As anticipated from past experience with pallidotomy for subthalamotomy-induced hemiballism and GPi DBS for Huntingtonâ€™s disease, high-frequency GPi DBS can be successful in treating hyperkinetic movement disorders refractory to dopaminergic blockade.

Movement disorders

Right hemichorea treated successfully by surgical removal of a left putaminal cavernous angioma.

Michael Sobstyl

Maciej Jakuciński (none), Mirosław Ziębek (none), Wojciech Górecki (none)

Introduction: There are only a few reports observing movement disorders like hemidystonia, hemichorea or hemiparkinsonism due to cavernous angioma (CA) located in basal ganglia. The object of this study was to present a case of right hemichorea successfully managed by extirpation of CA located in the left putamen.

Methods: We report on 58 year-old-woman with a 9 years history of right sided hemichorea. The hemichorea of the right hemibody appeared spontaneously at age 49. The magnetic resonance imaging revealed a well-defined lesion with a central focus of reticulated high signal intensity surrounded by a rim of void signal, ensuring the diagnosis of CA. The surgery was proposed. The informed consent was obtained from the patient. The extirpation of CA was performed with microsurgical technique under general anesthesia. The postoperative course was uneventful.

Results: We observed gradual amelioration of right-sided hemichorea during hospital stay. Hemichorea subsided during subsequent postoperative months. The patient is completely free of dyskinesia at 24 months follow-up.

Discussion: In a very limited world-wide experience with CAs located in the basal ganglia presenting with hyperkinesias the microsurgical extirpation of this malformation is feasible and safe with subsequent amelioration of dyskinesia. The lesions located in the putamen may be even more surgically accessible than CAs localized in deeper structures like caudate nucleus.

Conclusions: Surgical extirpation of deep seated CAs may not only prevent the risk of intracerebral bleeding but also ameliorate movement disorders.

Movement disorders

Unilateral pallidal stimulation for the treatment of truncal and upper limb girdles dystonia.

Michael Sobstyl

Maciej Jakuciński (none), Mirosław Ziębek (none), Sebastian Dzierżewski (none), Wojciech Górecki (none)

Unilateral pallidal stimulation for the treatment of truncal and upper limb girdles dystonia.

Introduction: The aim of the study was to present a patient with truncal and upper limb girdles dystonia, who underwent unilateral GPi stimulation

Methods: We present a case of 54-year-old man with 11 years history of dystonia. In the first years the dystonia was confined only to paravertebral muscles in the upper thoracic region. In the following years dystonia involved symmetrically the truncal, abdominal, upper limb girdles musculature with lesser involvement of his neck by dystonic movements. After obtaining informed consent the patient was operated on under general anesthesia.

Results: The neurological status was assessed using Burke-Fahn-Marsden-Dystonia Rating Scale - BFMDRS. His disability and motor BFMDRS scores decreased from 15 and 33 to 2 and 4 scores at 12 months respectively. We abandoned the initially planned left-side procedure in this patient because of good control of trunk dystonia.

Discussion: For patients with disabling truncal dystonia, bilateral GPi DBS is the surgical procedure preferred by many neurologists and stereotactic neurosurgeons. The presented case confirms that unilateral procedure can be effective in some patients. Moreover, unilateral procedure can decrease the risk of complications related to a simultaneous bilateral surgery and also lower the risk of producing parkinsonism-induced features reported in some patients treated by bilateral DBS GPi for cervical or segmental dystonia.

Conclusions: Unilateral GPi stimulation may substantially decrease dystonic movements affecting the axial musculature.

Neuro-imaging

The Hyperdirect Pathway as it Pertains to Side Effects Associated with Deep Brain Stimulation

Kabilar Gunalan

(Consultant Fee, Company: Cameron C. McIntyre, Boston Scientific Neuromodulation, Paid consultant)

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Introduction: Deep brain stimulation (DBS) alleviates the symptoms of Parkinson's disease but its mechanisms are not well understood. An emerging pathway of interest, thought to be modulated by DBS therapy, is the hyperdirect pathway that travels from cortex to the subthalamic nucleus (STN). Previous studies in rodents have shown antidromic activation of this pathway, resulting in modulated cortical activity.

Furthermore, Frankemolle et al. (Brain, 2010) have noted cognitive-motor side effects in patients implanted with DBS electrodes using stimulation settings determined clinically

(Clinical). These impairments improve by using settings that target the dorsal STN and neighboring white matter fibers (Model). In this study, we used tractography to understand which hyperdirect fiber pathways and cortical regions are associated with the cognitive side effects in the Frankemolle study. **Methods:** A volume of tissue activated (VTA), estimated using the stimulation settings, was calculated for each of the 10 patients' Clinical and Model settings. The VTAs were mapped onto a common brain and, subsequently, diffusion-tensor-based probabilistic fiber tractography was performed using each VTA as a seed point. **Results:** Preliminary results show that the Clinical VTAs have more fibers terminating in frontal cortical regions than the Model VTAs. **Discussion:** These fibers may account for the cognitive side effects associated with the Clinical settings, providing further evidence that modulation of the hyperdirect pathway is the mechanism by which DBS induces wide-scale network effects.

Conclusions: We used tractography to show that the cognitive side effects, induced by DBS, are associated with direct connections to frontal cortical regions.

Neuro-imaging

Segmentation of the Human Caudate Nucleus in AC-PC Space

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Introduction: Although the caudate is not part of the classical auditory pathway, recent publications indicate that a segment of this structure, area LC, may play a key role in tinnitus perception, a specific auditory phantom percept. Given this new view and the opportunity for further study in humans during functional neurosurgery, a new way of describing the caudate in surgical terms is needed. Analysis of future recording and stimulating experiments in and around area LC will likely be referenced to AC-PC coordinates.

Methods: High-resolution 1.5T MR images from 34 human subjects were analyzed. Segmentation and volumetric analysis of the caudate was performed on the BrainLab surgical planning workstation.

Results: The caudate was reliably subdivided into three anatomic regions relative to the AC-PC plane: 1) Area LC = region anterior to AC and above AC-PC plane, 2) Area PLC = region posterior to AC, and 3) Area ILC = region inferior to AC-PC plane. Area LC had a mean volume of 2.86 ± 0.55 cm³ on the right and 3.08 ± 0.60 cm³ on the left. Other analyses will be presented.

Discussion: The human caudate can be segmented in AC-PC coordinates familiar to stereotactic surgeons. A similar strategy for anatomic subdivision of the putamen has been useful in discussions of the role of that structure in Parkinson's disease.

Conclusions: This novel, surgically oriented subdivision of the caudate nucleus will provide a more consistent framework for organizing results of anatomical and physiological studies of this input structure to the basal ganglia.

Neuro-imaging

Revisiting finger somatotopy in the human motor cortex

Kai J. Miller

Eberhard Fetz (none), Jaimie M. Henderson (none), Jeffrey G. Ojemann (none), Paul S. Kalanithi (none)

Introduction: Initial studies by Penfield and colleagues, using intra-operative cortical stimulation suggested that individual fingers are represented at distinct locations on the pre-central gyrus. However, more recent work using functional imaging, lesion analysis, as well as axonal tracking and microelectrode recordings in non-human primates has led to the view that representation within the hand area of the homunculus is broadly distributed and overlapping between fingers.

Methods: We recorded the potential from subdural electrocorticographic (ECoG) electrode arrays in 8 human subjects while they performed simple finger movements during several second cues. Two correlates of population-scale physiology were extracted from the power spectrum of these potentials: first, the band-pass filtered "beta-rhythm" power between 12-20Hz was isolated; secondly, broadband shifts in the power spectrum, across all frequencies, were captured using a singular value decomposition (this has been shown to be a coarse correlate of neural population firing rate). For each of these, periods of movement were compared with periods of rest to obtain spatial maps of significant change.

Results: Broadband spectral changes show largely non-overlapping representation between different fingers, while the distribution of change in the beta rhythm overlaps almost completely in all cases.

Discussion: These findings point to a more well-delineated representation than recent studies would suggest, and reinforce the Penfield-style organization of the human hand motor homunculus.

Conclusion: Broadband ECoG changes during movements of individual fingers reveals distinct representation for different fingers in the human peri-central motor cortex.

Neuro-imaging

Creation of a Novel Interactive Tool for Computer-Assisted Multi-Modal Trajectory Planning

Abbas F. Sadikot

Bruce Pike (none), Silvain BÃ©riault (none)

Introduction. Frame-based or frameless approaches to deep brain targets require planning of insertion trajectories designed to mitigate risk of hemorrhage and loss of function. Currently, this is done empirically by manual inspection of imaging data. We propose an intuitive software framework for computer-assisted trajectory planning, applied initially to insertion of deep brain stimulator (DBS) electrodes.

Methods. Our framework accepts the following user-inputs: a target point (e.g. subthalamic nucleus), a set of surgical constraints (e.g. avoidance of blood vessels, cerebral sulci, ventricles), and multi-modal patient datasets (T1-weighted, T2-weighted, susceptibility-weighted and time-of-flight MR images). These datasets are automatically processed to extract a list of entry points after definition of a broad hemispheric or lobar search-space avoiding critical brain areas (e.g. primary sensorimotor and speech areas). An automatic algorithm aggregates the many requirements into a meaningful ranking of optimized trajectories.

Results. Thousands of trajectories are processed in <4 minutes. The problem is reduced to well-defined patches of best-ranked trajectories, presented to the surgeon for evaluation using an intuitive color-scale overlaid onto a 3D reconstructed cortex. A retrospective analysis on 15 DBS cases reveals that automatic planning can provide alternative trajectories further away from vessels or sulci compared to manual planning alone. This novel method may improve insertion safety, and reduce surgical time. A prospective analysis is underway.

Discussion and Conclusion. Using high computational power, our framework provides rapid, objective optimization of many customizable constraints across dense, multi-modal, datasets. The tool allows efficient optimization of patient-specific DBS lead trajectories, and can be generalized to trajectory planning for biopsies, endoscopy, insertion of depth electrodes, and approach corridors to deep-seated tumors.

Neuro-imaging

Brain surface localization of subdural strip electrodes using intraoperative fluoroscopic imaging

Nathan C. Rowland, M.D., Ph.D.

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INTRODUCTION: In functional neurosurgical procedures, temporary subdural strip electrodes (SSE) are often inserted to capture local field cortical activity for physiologic localization. Several methods exist to register SSE contact coordinates relative to brain surface landmarks, however their accuracy has not been extensively tested. We tested the accuracy of a method of projecting electrode contact locations onto brain surface renderings using intraoperative 2D images.

METHODS: Brain surface representations of five patients were rendered from preoperative MRI using statistical parametric mapping (SPM) algorithms in MATLAB. Bony landmarks from intraoperative lateral fluoroscopic images (LFI) with SSE contacts in situ were used to constrain the superposed surface. Three-dimensional coordinates in the AC-PC space were recorded for each contact and compared to coordinates obtained from an intraoperative CT image computationally fused to the preoperative MRI.

RESULTS: The A-P localization of the SSE contacts using only LFI was highly variable ($18.8 \hat{\pm} 13.9$ mm, mean distance from CT-derived coordinates $\hat{\pm}$ std). The localization of coordinates in the medial-lateral and vertical planes, however, was more accurate ($4.7 \hat{\pm} 8.9$ mm and $2.3 \hat{\pm} 8.6$ mm, respectively).

DISCUSSION: Superposition of SSE contacts detected by LFI onto rendered MR images has significant potential inaccuracies.

CONCLUSIONS: To improve accuracy of localization of SSE contacts using intraoperative fluoroscopy, future algorithms should incorporate coregistration of bony and frame-based landmarks seen on both preoperative CT and intraoperative fluoroscopy (such as frame pins) as well as additional xray views to further constrain the best fit of electrode location to brain surface.

Neuro-imaging

Trigeminal neuralgia secondary to a giant Virchow-Robin space – A case report with neuroimage.

Manish Ranjan

Christopher.R. Honey (none)

Introduction

The Virchow-Robin spaces are pial-lined interstitial fluid filled structures that accompany penetrating arteries and arterioles as they enter the cerebral substance. Occasionally they may become strikingly enlarged and cause mass effect. We present a rare case of trigeminal neuralgia (TN) secondary to dorsal pontine giant Virchow-Robin space (GVRS).

Method

Case report and relevant literature review.

Results

A seventy five year old man presented with a four year history of intermittent touch induced severe lancinating pain in the V1 dermatome. He did not have focal neurological deficits. MRI revealed a large non-enhancing multiple cystic lesion identical to CSF signal intensity on all sequences located in the right side of his dorsal pons and middle cerebral peduncle (with mass effect and bulging in to the 4th ventricle). There was no vascular compression at the trigeminal root entry zone. His pain was controlled with medication and surgery was deferred.

Discussion

GVRSs are common in the mesencephalothalamic region. There are a few case reports of symptomatic GVRS requiring surgery to relieve mass effect and hydrocephalus. We believe long standing compression and consequent demyelination of the trigeminal pathway may be the etiology of TN in this case.

Conclusion

To the best of the authors'™ knowledge, this is the first reported case of GVRS causing TN and clinicians should be aware of the neuroimaging characteristics of this rare but important entity.

Neuroprosthesis

Chronic non-isochronous beta band cerebellar DBS improves recovery from ischemia in a rodent model

Andre Machado

(Industry Grant Support, Company: Intellect Medical), (Industry Grant Support, Company: Medtronic), (Stock or Shareholder, Company: Intellect, Cardionomics and ATI. Intellect was acquired by Boston Scientific), (Consultant Fee, Company: Monteris, IntElect)

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Introduction

We have previously shown the effects of sustained and chronic dentatohalamocortical stimulation on cortical excitability and post ischemia recovery in a rodent model. This work explores the effects of a novel pattern of chronic beta band dentatohalamocortical stimulation combined with motor training on post-stroke recovery in rodents.

Methods

Twenty-three LE rats were trained in the pasta matrix task and underwent endothelin-1 (ET-1) injections in the motor cortex contralateral to the dominant paw and contralateral to a deep cerebellar electrode. Rats were matched according to stroke severity in the following groups: ISOSTIM (continuous isochronic 30 Hz stimulation), NONISOSTIM (30 Hz stimulation and superimposed irregular stimulation) and SHAM. At the end all animals underwent transcardiac perfusion for histological examination of stroke volume and electrode location.

Results

No inter-group difference in task performance was observed prior to stimulation onset. At the end weeks three and five, the ISOSTIM group retrieved an average(SD) of 26.7(7.6) and 27.0(8.7) pasta pieces, respectively, with the affected paw, while the NONISOSTIM group retrieved 28.2(5.0) and 30.4(7.5) pieces. SHAM animals retrieved 22.3(9.7) and 22.1(9.3) pieces. Pair-wise comparison revealed NONISOSTIM to be significantly better than SHAM ($p=0.015$) on motor rehabilitation at week 5.

Discussion

The results indicate that this novel pattern of stimulation (30 Hz with superimposed irregular stimulation) can effectively enhance neurorehabilitation. The pattern resembles Hebbian facilitation paradigms and suggests long term potentiation-mediated plasticity.

Conclusion

Chronic dentatohalamocortical DBS with a novel stimulation paradigm is promising for stroke rehabilitation.

Neuroprosthesis

Deep Brain Direct Current Stimulation Alters Auditory Response Properties

Joaquin De Rojas

Joaquin De Rojas (none), Roy Hamilton (none), Steven Siegel (none)

INTRODUCTION: Although deep brain and transcranial direct current stimulation are currently being used as investigative tools and therapies for a variety of neurological conditions, their mechanisms remain poorly understood. Importantly, no animal studies to date have directly measured physiological changes associated with direct, low-current brain stimulation.

METHODS: Twenty-four mice were assigned to anodal, cathodal, and sham groups and were implanted with electrodes in left auditory cortex. Mice underwent direct current stimulation for 20min at 20microAmps. Auditory evoked potentials were recorded pre-stimulation, 1hr, 1wk, and 2wk post-stimulation. EEG was analyzed for amplitude/latency of P1, N1, and P2 signals. We assessed EEG power and intertrial coherence using event-related spectral perturbations.

RESULTS: In the anodal condition there was significant reduction in delta, theta, and alpha power that persisted through the two-week timepoint. In the cathodal condition there was significant reduction in delta that persisted through the one-week timepoint and reduction in theta and alpha power observed at the one-hour timepoint (all p values < .05). There were no differences within the sham group and N1 amplitudes and latencies did not change across time for any group.

DISCUSSION: Observed reductions in low frequency power bands after direct current stimulation were consistent with recent clinical studies (Keeser et al., 2010). Attenuation of low frequency power may be associated with improved cognitive function and increased BOLD signal changes (Hlinka et al., 2010).

CONCLUSION: Our approach provides a means to examine the use of deep brain direct current stimulation to enhance brain function in animal models.

Neuroprosthesis

Epidural Spinal Cord Stimulators: Applications and Directions

Andrea Brock

Peter E. Konrad (none), Vivian K. Mushahwar (none)

Introduction: People with complete or incomplete spinal cord injury (SCI) are prone to health complications such as infection and decreased ambulation. Epidural spinal cord stimulation (ESCS) shows promise in facilitating functional recovery and improving vascular circulation.

Methods: PubMed was searched for English articles published 2000-present using the terms: epidural, electrical, stimulation, stimulator, and spinal cord. Studies utilizing ESCS for neurogenic pain and review articles were excluded. Fifty-four human studies were returned of which 17 described ESCS applied to functional problems.

Results: ESCS applications can be categorized into motor and autonomic. In patients without normal cough mechanism, ESCS allowed greater pressure generation and higher peak airflow rates. When used to elicit lower extremity movement, ESCS resulted in smoother stepping patterns, greater supported body weight, increased speed and endurance, and a reduced sense of effort. Varying the frequency of stimulation determined motor output; 50-100Hz reduced spasticity, 25-50Hz produced rhythmical flexion/extension, and <15Hz extended the knee. For bladder control, ESCS decreased urinary frequency, increased voiding volume, and subjectively decreased urinary urgency. Finally, ESCS decreased pain and improved blood flow in patients with vascular disease.

Discussion: ESCS has the potential to alleviate many ailments affecting those with SCI. Restoring cough, improving ambulation, and increasing bladder control enhances independence for daily activities. For patients with vascular insufficiency, decreasing ischemic pain, improving blood flow, and subsequently improving ulcer healing potentially postpones or renders amputation unnecessary.

Conclusion: The successful application of ESCS to motor and autonomic functions builds the foundation for future expansion to other modalities.

Pain therapies

Initial Clinical Results of DRG Stimulation for the Treatment of Chronic Pain

Robert Levy, M.D., Ph.D.

(Honorarium, Company: Bioness, Codman, Medtronic Neurological, St. Jude Medical, Spinal Modulation, Vertos Medical),
(Consultant Fee, Company: Bioness, Codman, Medtronic Neurological, St. Jude Medical, Spinal Modulation, Vertos Medical),
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Introduction: Chronic neuropathic pain can be challenging to treat with current therapies. Stimulation of the dorsal root ganglion (DRG) is a potentially potent alternative. This study evaluated the effects of DRG stimulation on subjects with chronic neuropathic pain.

Methods: 31 subjects with neuropathic pain for at least six months were enrolled in 2 prospective studies. Custom leads were percutaneously implanted at the target DRGs and connected to a fully implantable neurostimulation system (Spinal Modulation, Menlo Park, CA). Pain was measured on a Visual Analog Scale prior to treatment and at scheduled follow-ups. Secondary outcome measures were also evaluated.

Results: 31 subjects with several indications including FBSS and CRPS have been enrolled to date. Significant reductions in pain were observed through six months of follow-up. 67% of all enrolled subjects experienced > 50% pain reduction. 86% of patients with leg pain had >50% relief. Adverse events were rare with a 3.6% lead migration rate. Patients reported minimal changes in paresthesias due to postural changes.

Discussion: Early results indicate that DRG stimulation may be a promising alternative for patients with pain conditions that are typically hard to treat with conventional SCS. This study shows that paresthesias can be directed in a selective and specific manner with particularly high success in patients with leg and foot pain. The evidence of cross dermatomal coverage shows unique promise for patients with FBSS.

Conclusion: The results of these trials suggest that DRG stimulation may be effective in treating chronic neuropathic pain.

Pain therapies

Facial Pain Diagnostic Questionnaire

Kim J. Burchiel, M.D.

Shirley McCartney, Ph.D. (none)

Objectives: To explore the utility of a facial pain diagnostic questionnaire and expert system in the diagnosis of facial pain.

Methods: A facial pain questionnaire was developed and linked to an artificial neural network (ANN) program trained to recognize a set of diagnostic categories.

Results: From 12/06 to 12/11, 765 data sets were entered from patients in our facial pain clinic. Of these, 568 (365 females) were used to train the ANN on an in-house server. In 487 cases, the diagnosis reached was the same as that of the senior author (86% accuracy). For the diagnosis of TN1 (typical trigeminal neuralgia), the sensitivity was 0.9683, and specificity 0.8286.

Conclusions: An ANN can make the diagnosis of TN1 accurately, with high sensitivity and specificity.

Pain therapies

Pulsed radiofrequency as an optional treatment to chronic migraine

Tiago Freitas

Freitas T.S. (none), Kessler I. (none), Moura F.A. (none), Silva H.Y.W. (none), Valente F.A. (none)

Introduction: Chronic migraine (CM) is a disabling neurologic disorder and constitutes Migraine's natural evolution in approximately 3% to 14% of patients. The treatment options for this difficult to manage syndrome includes pharmacological approaches and alternative non-pharmacological procedures such as botulinum toxin and neuromodulation procedures (occipital and occipital/supraorbital peripheral nerve stimulation). In this context, pulsed radiofrequency (PRF) has gained popularity in pain management due to its minimally invasive nature and a possible neuromodulation effect. The aim of this study was to evaluate the use of PRF on patients with CM.

Methods: 24 CM patients without response to previous treatment were subjected to PRF, done in 3 cycles of 120 seconds in bilateral occipital and supra-orbital nerves. Patients' specific headache measurements were assessed through number of days with moderate or severe intensity headaches, number of migraine days and number of migraine episodes. Response rates were defined as 30% reduction in baseline parameters. Follow-up evaluation was at 1 month, 3 months and 6 months post-procedure.

Results: 10 patients (41%) showed a lasting (6 months of follow-up) improvement greater than 30% in specific headache measurements.

Discussion: CM is not uncommon in the general population and is the most disabling form of migraine. Notoriously resistant to drug treatment, any progress in CM management is thus appreciated.

Conclusion: PRF of bilateral frontal and occipital nerves promises to be an alternative option for management of CM. A longer follow-up, randomized and placebo-controlled studies are necessary to confirm this hypothesis.

Pain therapies

Utilization of Spinal Cord Stimulation in patients with Failed Back Surgery Syndrome

Shivanand P. Lad

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Introduction: Post-laminectomy pain syndrome (aka Failed back surgery syndrome (FBSS)) represents a major source of chronic neuropathic pain. Several landmark studies in the field have demonstrated superior pain relief, improved quality of life and functional capacity compared to Spinal re-operation. The goal of this study was to determine real world utilization of SCS in this population and compare complications, charges and healthcare resources in a large, independent cohort of FBSS patients undergoing surgical intervention.

Methods: The Reuter's™ MarketScan database was utilized to perform a retrospective, cross-sectional, population-based study. FBSS patients who underwent SCS or Spinal reoperation (laminectomy, fusion, revision fusion) between 2000 and 2009 were identified. Logistic regression analysis was used to examine long-term complication rates. Propensity score matching was utilized to compare a matched cohort of patients, examining hospital charges and healthcare resource utilization.

Results and Discussion: The study cohort comprised a total of 16,455 FBSS patients, with a total of 395 patients undergoing SCS implantation (2.4%) and the remaining 16,060 undergoing spinal re-operation (97.6%). Complication rates at 90 days were significantly lower for SCS compared to Spinal re-operation (6.5% vs 14.4%, $p < 0.0001$). In a matched cohort of patients, hospital charges were lower for SCS compared to Spinal re-operation (\$31,210 vs \$40,433, $p = 0.02$). Use of outpatient services, ER and medication charges were not significantly different between the two groups.

Conclusion: Despite prior data suggesting improved functional outcomes, lower complications and hospital charges with SCS compared to Spinal re-operation, only a small percentage of FBSS patients currently receive SCS.

Pain therapies

Microvascular Decompression: Re-operation Rates and Healthcare Resource Utilization

Anand Veeravagu

Anand Veeravagu, MD (none), Beatrice Ugiliweneza, MD (none), Bowen Jiang, BS (none), Chirag G. Patil, MD (none), Kevin Huang, BS (none), Maxwell Boakye, MD (none), Melanie G. Hayden Gephart, MD MAS (none), Paul S. Kalanithi, MD (none), Shivanand P. Lad, MD PhD (none)

Introduction: Microvascular decompression (MVD) is a well-accepted technique for the surgical management of various cranial neuropathies. While many studies have examined the outcomes of MVD in single-center trials, we sought to determine the re-operation rate in a large, independent cohort of patients undergoing MVD surgery.

Methods: The Reuter's MarketScan database was utilized to perform a retrospective, population-based study. Patients who underwent MVD for trigeminal neuralgia, hemifacial spasm or glossopharyngeal neuralgia between 2000 and 2009. Of the 278 MVD procedures identified, all patients with less than 2 years of post-operative follow-up data were excluded. The records of the remaining 113 patients were analyzed using a logistic regression analysis examining long-term complication and re-operation rates, type of re-operation and outpatient healthcare resource utilization.

Results and Discussion:

The study sample included 278 patients with a total of 113 patients with >2 year follow-up. The mean age was 56 years, 67% female, 68% Commercial insurance, 87% with low comorbidities (Charlson index= 0) and mean follow-up of 4 years. The 1, 2 and long-term re-operation rates were 2.7%, 3.5% and 4.4%, respectively. Post-operative complications totaled 8.0% at 90 days. Re-operation consisted of redo MVD (3.5%), balloon decompression (1.8%), and radiosurgery (0.88%). Average time to re-operation was 3.8 years and 2 year follow-up resulted in hospital charges totaling \$9018, outpatient services of \$9384, and medication charges of \$4906.

Conclusion: In this large, retrospective study, MVD remains a robust procedure that is well-tolerated. Repeat MVD remains the first-line choice for those requiring re-operation.

Pain therapies

Peripheral nerve stimulation for neuropathic pain caused by leprosy

Tiago Freitas

Akamine A.I.L. (none), Freitas T.S. (none), Kessler I. (none), Moura F.A. (none), Neto O.R.M. (none), Valente F.A. (none)

Introduction: Leprosy is an infectious disease that affects mainly the skin and peripheral nervous system. Associated chronic painful neuritis causes considerable functional limitation, and its treatment may involve surgical decompression in cases resistant to conservative treatment. Although considered an excellent option, some patients persist with neuropathic pain after surgery. This study focuses on the use of peripheral nerve stimulation in management of patients previously submitted to all available treatments for chronic leprosy neuropathy.

Methods: 15 leprosy patients with chronic neuropathic pain unresponsive to medication and surgical decompression were selected for a trial implant. All patients underwent prior testing for 7 days and were assessed with Visual Analogic Scale (VAS) and neuropathic pain scale (NPS). Those with at least 50% scale improvement received a permanent device. Follow-up evaluated VAS and NPS at 7 days, 1 month, 3 months and 6 months post-procedure.

Results: 8 patients received a permanent device. Among these, 6 patients (75%) showed at least a 50% improvement in VAS and NPS while 2 patients showed a 30% scale improvement. All improvements maintained during 6 months follow-up. There were 2 lead migration and no infection

Discussion: Leprosy remains a public health problem in developing countries and is a major cause of peripheral neuropathy worldwide. Furthermore, it is responsible for serious limitations to patients despite treatment exhaustion.

Conclusion: Peripheral nerve stimulation is an important additional tool in management of chronic neuropathic pain secondary to leprosy. Longer follow-up and a greater number of patients are necessary to confirm its potential benefit

Pain therapies

Scarring Under Paddle Electrodes and Implications for the Relationship Between Impedance Measurement

Jay L. Shils, PhD

Jeffrey E. Arle, MD, PhD (Disclosure: Consultant Fee Company: St. Jude Medical), Kris W. Carlson (none), Longzhi Mei (none)

Introduction:

Scar formation under and around paddle electrodes used in SCS is a potential concern for consistency in delivered therapy. It has been assumed that impedance measurements give useful feedback on the local scar environment of paddle contacts and are a reliable gauge by which programming changes can be made.

Methods:

We created a complex 3-D FEA model of the spinal cord (SC) and a common paddle lead. Complex scar patterns were then placed between the lead and dura. Two common compensation methods were also studied.

Results:

Scarring distorts the potential field in three dimensions and bears little relation to the impedance readouts of the systems. Increasing the voltage on the scared electrode does not necessarily bring the potential field back to its original shape and can even generate new unwanted high current density regions.

Discussion:

Impedance measurements are primarily a function of the conductance of the scar and dura between the two contacts, not from the lead to the cord. More importantly, they do not necessarily reflect accurate information about current patterns ultimately reaching the cord. We find the relationship between scar thickening related impedance changes and current delivered to the dorsal columns are nonlinearly related.

Conclusion:

These findings call into question the usefulness of impedance measurements in driving programming changes, (though still helpful in assessing electrical continuity), and the potential benefits of constant-current stimulation systems when highly resistive tissue (dura and scar) is between the electrodes and spinal cord.

Pain therapies

Trigeminal Neuralgia Occurs and Recurs in the Absence of Vascular Compression

Kim J. Burchiel, M.D.

Benedict B.T. Taw (none), Stephen E. Griffith, M.D. (none)

Objectives: Microvascular decompression (MVD) is widely accepted as the surgical procedure of choice for medically intractable patients with trigeminal neuralgia (TN). However, past experience would indicate that TN can occur in the absence of neurovascular compression (NVC), and that over time a substantial number of patients will have recurrence of TN despite an initially successful MVD.

Methods: High resolution trigeminal nerve imaging was reviewed in 134 patients with TN1 using MRI (BFFE), and MRA, with 3D image reconstruction (Osirix).

Results: Imaging revealed that 80 patients (60%) had ipsilateral NVC, 25 (19%) had bilateral NVC, 14 (10%) had no NVC, and 15 (11%) had equivocal NVC. Fourteen patients with unilateral TN1 showed no ipsilateral NVC (10%), seven patients with bilateral TN1 showed no NVC on one side, and five patients who had an initially successful MVD for TN presented with recurrent symptoms, did not have recurrent ipsilateral NVC.

Conclusions: Imaging and surgical exploration confirmed no NVC in a group of patients with unilateral TN, bilateral TN, and recurrent TN after MVD. These results suggest that in some patients, the etiology of TN is not due to NVC.

Pain therapies

A Study of Intrathecal Pump Accuracy and the Effects of Temperature on Rate of Administration

Tyler Ball

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Introduction:

The SynchroMed pump (Medtronic) is the only FDA approved programmable intrathecal pump. Recently, the Prometra pump (Medasys) has entered trials with a dual-valve design to mitigate the effects of environmental conditions on delivery. The purpose of this study is to compare accuracy while varying temperature.

Methods:

Pumps were placed in an incubator at 22, 37 or 40°C while a digital scale recorded mass at one minute intervals. Catheter tips were placed at the bottom of a 10cm column of water to simulate CSF pressure.

Results:

Both pumps under-administered at room temperature. When heated to body temperature, there was a transient (4-5 hr) increase in flow. When programmed to deliver 0.1 mL/day at body temperature, the Prometra delivered 0.100 ± 0.004 mL/day, while the SynchroMed delivered 0.102 ± 0.004 mL/day. At 40°C, the Prometra did not have a significant increase in flow rate, but the SynchroMed showed a 7% increase.

Discussion:

Both pump designs demonstrate transient initial overdelivery while equilibrating to body temperature. At body temperature, the dual-valve design demonstrated higher accuracy and less sensitivity to ambient temperature in the range from normal to febrile states. Controlling temperature for pumps and medication prior to implantation may lead to a more accurate flow rate in the hours immediately following surgery.

Conclusions:

A dual-valve design may be more accurate at varying temperatures, and use of a warmer to bring the pump and medication to body temperature prior to implantation may be helpful for producing reliable delivery in the immediate postoperative period.

Pain therapies

FLAT-PANEL FLUOROSCOPY WITH O-ARM GUIDED PERCUTANEOUS RADIOFREQUENCY CORDOTOMY

Parag G. Patil

Parag G. Patil (none)

INTRODUCTION: Percutaneous radiofrequency cordotomy (PRFC) involves controlled ablation of the anterolateral quadrant of the spinal cord, thereby relieving pain. Evolving from a morbid open surgery, the procedure has been modernized through the application of physiological target confirmation, well-regulated thermal ablation, and CT-guided imaging. This study evaluated the utility of a new high-resolution, portable flat-panel fluoroscopic imaging technology in PRFC.

METHODS: PRFC was performed utilizing the O-Arm[®] Imaging System to augment established physiological targeting and radiofrequency ablation techniques in six patients with intractable unilateral cancer pain.

RESULTS: The O-Arm[®] Imaging System allowed clear visualization of the radiofrequency needle and the spinal cord during the procedure. All patients experienced 90-100% reduction in unilateral pain following percutaneous cordotomy, without complication. Patients survived 2 to 8 months with persistent pain relief ranging from 50-100%.

DISCUSSION: Portable flat-panel fluoroscopy allows high-resolution, readily updated image guidance during PRFC, comparable to intraoperative CT imaging together with fluoroscopy, with analgesia producing significant improvement in patient quality-of-life.

CONCLUSIONS: Utilization of this widely available technology may assist neurosurgeons to provide an important analgesic intervention in centers possessing the imaging technology. PRFC remains an important tool in the neurosurgical armamentarium to combat cancer pain.

Pain therapies

Internet self-diagnosis of trigeminal neuralgia

Rita Nguyen

R Nguyen (none), ZHT Kiss (none)

Introduction

Because the diagnosis of trigeminal neuralgia (TN) is made by history, one would expect that a questionnaire filled in by the patient could make the diagnosis. Such an on-line questionnaire (<https://neurosurgery.ohsu.edu/tgn.php>) was developed by the Oregon Health Sciences Centre (OHSU) and validated on a subset of their patients. To assess its utility, we compared diagnoses made by the questionnaire to that made by an experienced clinician (â€˜gold standardâ€™™).

Methods

All patients with craniofacial pain presenting to a neurosurgery clinic independently filled in a paper version of the questionnaire. The neurosurgeon was blinded to the questionnaire and made a diagnosis based on usual clinical assessment. Sensitivity and specificity of the questionnaire was determined in relation to clinical evaluation.

Results

Of the 97 patients evaluated, the clinical diagnoses were typical TN (58.8%), atypical TN (28.9%), atypical face pain (7.2%), with the remainder having other pain/headache syndromes. Over half of the patients (52) received a diagnosis using the questionnaire that was different to that obtained by clinical evaluation. The questionnaire had a sensitivity of 0.72, specificity of 0.50 for diagnosing TN, and sensitivity of 0.60, specificity of 0.74 for diagnosing other craniofacial pains.

Discussion

The diagnosis of facial pain can be complex. A questionnaire gives patients the opportunity to become informed regarding various diagnoses; however, a formal evaluation by a specialist is necessary to direct appropriate management.

Conclusion

A web-based questionnaire is insufficient to make an accurate diagnosis of TN.

Pain therapies

PULSED RADIOFREQUENCY OF SYMPATHETIC LUMBAR PLEXUS VERSUS SYMPATHETIC BLOCK IN THE MANAGEMENT OF LOW

Tiago Freitas

Ferreira I.C. (none), Freitas T.S. (none), Kessler I. (none), Neto O.R.M. (none)

Introduction: Complex Regional Pain Syndrome (CRPS) type 1 is a neuropathic pain syndrome which clinical treatment involves oral medications, physiotherapy and other alternative therapies. The purpose of this study was to compare two safety options : pulsed radiofrequency(PRF) or sympathetic blocks (SB), and their efficacy in the different aspects of this neuropathic pain and in quality of life of patients suffering from this disease.

Methods: 40 randomized patients to receive PRF or SB in lower limb CRPS type 1. They were prospectively evaluated with VAS scores, neuropathic pain scale and RAND SF-36 (Research and Development Short Form Health Survey) in a follow up of 7 days, 3-6-12 and 15 months.

Results: There were similar reductions from baseline in various pain scores. In the PRF group these results were statistically more consistent with the follow up period with the burning pain ($P < 0.05$). The other pain parameters and RAND SF-36 scale had similar results in both groups.

Discussion: CRPS type 1 is an neuropathic pain syndrome usually of difficult treatment and many patients evolve to the necessity of interventional procedures. PRF has gained evidence in pain management due a possible neuromodulation effect.

Conclusion: PRF appears as a technique with similar results when compared with the sympathetic block. Only one pain outcome (hot pain) was statistically significant and this difference was insignificant to the final result. Once a higher-cost procedure with too few benefits, this particular difference did not affect the quality of life (RAND SF-36).

Pain therapies

Trigeminal Neuralgia Diagnostic Questionnaire

Kim Burchiel

Shirley McCartney, Ph.D. (none)

Introduction:

A classification scheme for facial pain syndromes describing 7 categories has previously been proposed. Based on this classification scheme and a binomial (yes/no) facial pain questionnaire, we previously designed and trained an artificial neural network (ANN). We report the ANN system's ability to recognize and correctly diagnose patients with different facial pain syndromes.

Methods:

Over a 5-year time span (December 2006-December 2011), 765 patients with facial pain were consented and responded to an online facial pain questionnaire at the time of their initial clinic visit. The ANN determined a diagnosis based on individual patients responses to the questions. After interview, an independent diagnosis was assigned to each patient.

Results:

Of the 765 consented subjects, it was determined that 568 of the patient responses were useable by the ANN. There were 365 female (64.3%) respondents and average age was 58.34 ± 12.15 years. Overall, the ANN predicted the correct diagnosis for 487 of 568 patients (85.5%). Type 1 trigeminal neuralgia (TN1) was identified with a sensitivity of 0.9683, and a specificity of 0.8286.

Discussion:

Using a diagnostic questionnaire and a trained ANN, we were able to differentiate seven forms of facial pain with high reliability. In particular, trigeminal neuralgia (TN1) could be diagnosed with high sensitivity and specificity. This questionnaire has been anonymously accessible on the www for more than five years. This resource may allow the self-diagnosis of facial pain, and direct patients to appropriate care.

Conclusion:

The OHSU trigeminal neuralgia diagnostic questionnaire has been shown to be an effective diagnostic tool.

Pain therapies

Influences on operative time and patient outcome in thoracic spinal cord stimulator placement

Erika Petersen

Blake C. Phillips (none), Erika A. Petersen (none), Jared Garrett (none), John Garrett (none), Veronica Williford (none)

Introduction:

Precise placement of thoracic spinal cord stimulator (SCS) paddle electrodes is essential for successful stimulation. Surgical techniques include placement of electrodes under local anesthesia and conscious sedation with intraoperative testing and placement under general anesthesia (GA) using fluoroscopy and neurophysiologic testing including EMG and somatosensory evoked potentials (SSEPs). This study evaluates these techniques in terms of operative time and patient outcome.

Methods:

A retrospective study of 56 consecutive patients undergoing thoracic laminectomy for SCS paddle electrode placement identified 29 cases performed under general anesthesia with SSEP testing. There were 22 cases performed under GA without SSEPs and 5 cases under local anesthesia. Data collected included operative indication, operative time, complications, pain scores, and frequency of stimulator reprogramming sessions.

Results:

Average operative time required for SCS surgery was $95\hat{\pm}26$ for GA+SSEP cases and $103\hat{\pm}25$ minutes for GA cases without SSEP monitoring. There was no statistically significant difference in operative time when comparing initial placements and revisions. Presence of a resident trainee during the case also did not affect operative time. 68.8% of patients undergoing GA cases without SSEPs and 72.0% of patients undergoing GA+SSEP cases reported improved VAS scores.

Discussion:

SCS placement required similar operative time using either local or general anesthesia and regardless of SSEP testing. Placement of electrodes under GA may be more comfortable for the patient and results in similar VAS decreases and operative time required.

Conclusion:

Placement of SCS electrodes under GA using SSEPs may be more comfortable for the patient, and results in similar pain control outcomes and operative time required.

Pain therapies

Theoretical Effect of DBS on Axonal Fibers of Passage

Jay L. Shils

Jay L. Shils, PhD (none), Jeffrey E. Arle, MD, PhD (none), Longzhi Mei (none)

Introduction:

Deep brain stimulation (DBS) is a widely used therapy in which electrical stimulation has potential effects on axons that originate outside the DBS target area yet pass through the activation field of the DBS electrode in addition to modulation of the intended neuronal target structure. The purpose of this study was to quantify these changes.

Methods:

Using the parameters of DBS firing frequency (f_a), the average intrinsic firing rate of the pre-synaptic cell (f_{c}), the maximum activating function location (L_{maxAF}), the propagation velocity of action potentials (V_{AP}), and the refractory time (T_r). We also simulated the system to corroborate whether this theoretical function could predict the what activity arrives at the post synaptic cell.

Results:

The derived function that determines the activity ultimately reaching the end of these axons is given as follows:

$$SNR = f_a / f_c [1 - 2f_a((L_{maxAF} / V_{AP}) + T_r)]$$

The predictability of the function was over 98% matched by the simulations.

Discussion/Conclusion:

These findings show that this function increases as either the L_{maxAF} or if f_a increases. However, if f_{c} is high enough relative to f_a , then the no reduction in f_{c} may be noted. This is largely due to the fact that APs exist within the axon for a very brief time, and if the cell's intrinsic average firing rate is approximately 1.5 times the stimulator frequency, then although the DBS signal gets through, so much intrinsic cell activity also gets through that the intrinsic activity is not reduced at all by the electrode signal. Thus the system is essentially a high pass filter.

Pain therapies

Spinal Cord Stimulation for Post-Orchiectomy Neuropathic Pain: Case Report

Erika Petersen

Ahmed Ghaleb (none), Diaa Bahgat (none), Erika Petersen (none)

Introduction

Post-operative neuropathic groin pain has been reported to occur after procedures including hernia repair, appendectomy, hysterectomy, and vasectomy. This pain often does not respond to medical therapy, and interventional procedures offer mixed results. We present a case of groin pain following orchiectomy that was resistant to conservative measures and treated with thoracic spinal cord stimulation (SCS).

Methods

The authors describe the case of a 46 year old male with chronic groin pain after undergoing orchiectomy. Pain control using medications including opioids and gabapentin was poor. A percutaneous trial of spinal cord stimulation using two octrode arrays centered at T10 provided complete pain relief. A surgical paddle electrode (Precision Plus, Boston Scientific, Natick, MA) was placed at T9-10 without complication.

Results

Stimulation immediately after implantation evoked paresthesias in the groin and into the left leg. Adequate relief of the groin pain was achieved. Visual Analog Scale pain score decreased from 7 prior to implantation to 3 at one month post-op. At 8 months after implantation, pain relief was maintained. Patient functional status improved.

Discussion

Spinal cord stimulation offers a good option to manage otherwise intractable neuropathic pain with the advantage of being testable, reversible, and adjustable. Stimulation in this case provided dramatic, sustained improvement in pain control.

Conclusion

We present SCS as an avenue for treating neuropathic groin pain. To our knowledge this is the first case of post-orchiectomy groin pain treated by spinal cord stimulation.

Psychiatric diseases

Single Neurons in the Human Subcallosal Cingulate Cortex Differentiate Emotion Categories

Adrian W. Laxton

(University Grants/Research Support, Company: Canadian Institute of Health Research)

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Introduction: Emotional information can be classified into distinct categories based on valence and arousal. The neuronal mechanisms underlying this type of categorization are not well understood. We identified for the first time single neurons in the human subcallosal cingulate cortex (SCC) that respond specifically to images representing distinct categories of emotional information.

Methods: Fifteen patients with major depressive disorder, undergoing SCC DBS to treat depression, enrolled in the study. During intraoperative microelectrode recording, participants sequentially viewed 50 images subdivided into 5 emotion categories based on valence and arousal. Single neuron activity was extracted and analyzed in relation to image presentation.

Results: SCC neurons were more likely to respond specifically to complex emotion categories than to valence or arousal alone ($\bar{t}= 33.6$, $p < 0.001$). SCC neurons were preferentially responsive to negative emotion categories ($\bar{t}= 16.2$, $p < 0.001$). The firing rates of neurons responsive to a specific emotion category increased by 92.5% or decreased by 47.8% relative to fixation frequency. Neurons responsive to a specific emotion category were not restricted to a specific location within the SCC.

Discussion: This is the first report of human single neuron activity in the SCC of depressed patients, and provides new insights into the neuroanatomical substrates of emotional information processing. Depression therapies that alter activity in this region may work by down-regulating an overactive and preferentially negative emotional processing bias.

Conclusions: SCC neurons are specifically responsive to images of particular emotion categories and preferentially responsive to negative emotion categories.

Psychiatric diseases

Bilateral GPe-DBS for Refractory Tourette Syndrome

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Introduction: Although frequently self-limited, when persistent, Tourette syndrome (TS) presents a high intractability rate. Ablative surgery presents a relatively low significant improvement and a high neurological morbidity. DBS for the treatment of TS was first performed by Visser-Vandewalle et al in 1999. We have previously suggested that GPe is hyperactive in TS. Based on this hypothesis, we performed bilateral GPe-DBS in nine consecutive TS patients.

Methods: Nine patients, 8M/1F, ages 18 to 47 years, refractory to the best conservative management, have been operated on. Preoperative assessment included MR, PET-scan or SPECT, neurological/neuropsychological/psychiatric evaluations, YGTSS and YBOCS, all of them repeated postoperatively. Target (central GPe) coordinates were obtained from IR MR coronal/axial slices, CT-scan and image fusion. Physiological mapping was performed through MER (2 patients) and macroelectrode stimulation. YGTSS and YBOCS were applied by a unique rater, being both patient and rater blind to the IPG status. Patients were videorecorded pre- and postoperatively.

Results: Target coordinates were usually 3.0-4.5mm posterior/3.0-4.0mm above/20.0-22.0mm lateral to AC. Postoperative MR was used to confirm adequate electrode positioning in every patient. The best stimulation parameters were: monopolar (most dorsal contacts), 2.5-3.5V, 100-160Hz, and 90-150usec. Mean follow-up period was 39 (2-95) months. Tics (YGTSS) and obsessive-compulsive behavior (YBOCS) improved a mean of 74% and 71%, respectively. Complications: asymptomatic perielectrode edema (n=1), transient depression (n=1).

Discussion and Conclusions:

The results reported support the hypothesis of GPe hyperactivity in TS and indicate that GPe-DBS provides symptomatic relief at least as good as the other techniques currently under trial.

Psychiatric diseases

Binge eating is attenuated by accumbens deep brain stimulation: a mechanistic approach in mice

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Introduction: Increased dopaminergic transmission in the nucleus accumbens (NAc) has been implicated in binge eating, a common feature of obesity. NAc deep brain stimulation (DBS) is hypothesized to attenuate binge eating by modulating dopaminergic receptors on medium spiny neurons. Thus, pharmacologic blockade of these receptors is hypothesized to blunt the effect of DBS on binge eating.

Methods: Mice (C57Bl/6) were implanted unilaterally with a bipolar electrode in the NAc (confirmed post-mortem). Following recovery, mice were provided high fat food (HF; 60% fat) for 1-hour daily. Once a stable level of binge eating was reached (>25% daily caloric intake), DBS (160Hz, 60us, 150uA) was administered during exposure to HF. Mice were then pretreated with a dopamine type 1 (D1R)-antagonist (SCH-23390; 0.075mg/kg) or D2R-antagonist (raclopride; 3mg/kg). Fos protein immunoreactivity was measured to examine neuronal activity regionally.

Results: Binge eating was significantly suppressed by NAc DBS ($p < 0.01$). c-Fos-IR was increased in the NAc ipsilateral to the DBS electrode ($p < 0.04$), and there was a trend contralaterally. There was no change in c-Fos-IR in the infralimbic cortex with DBS alone. Pretreatment with raclopride suppressed the action of DBS on binge eating by 51% ($p < 0.02$). Pre-treatment with raclopride and SCH-23390 resulted in a trend of increased c-Fos-IR in both the NAc and infralimbic cortex bilaterally.

Conclusions: Our findings implicate the NAc and dopaminergic system in binge eating. DBS amelioration of binge eating appears to be mediated in part by the D2R. Further studies incorporating optogenetic techniques will allow for cell-type specific dissection of this reward circuit.

Psychiatric diseases

Surgical Treatment of the Positive Symptoms of Schizophrenia

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Introduction: Schizophrenia is a highly prevalent psychiatric disorder. A significant number of these patients is refractory to the best conservative management, being aggressiveness the most common indication for surgery. Several surgical approaches have been used to treat this manifestation. Our usual approach was bilateral anterior calloso-cingulotomy+amigdalotomy. None of the patients so treated was improved from hallucinatory or delusional symptomatology. In 5 patients, having the preoperative SPECT shown hypermetabolism of bilateral prefrontal areas, we associated bilateral subcaudate tractotomy. We here report the results achieved in these patients in regard to the positive symptoms of their diseases.

Methods: Five male schizophrenic patients, ages from 23 to 56 years, all with a long-term history of disease characterized by hallucinations, delusions, agitation, aggressiveness, thought disorganization, and cognitive deficit, considered refractory to conservative management, were operated on. Preoperative assessment consisted of neurological, neuropsychological, and psychiatric evaluations, MR, and SPECT, all repeated postoperatively. Targets (bilateral amygdala, anterior calloso-cingulum, and subcaudate area) coordinates were obtained from IR coronal MR, CT, and image fusion. Under general anesthesia, without muscle relaxants, target macrostimulation was performed before radiofrequency lesioning.

Results: Postoperative MR showed appropriate placed lesions. All patients experienced immediate postoperative relief of aggressiveness, hallucinations and delusions, that persist after a long-term follow-up in 4 patients. The fifth patient still present occasional paranoid delusions associated with unprovoked aggression.

Discussion/Conclusions: The impressive reduction of hallucinations and delusions in four out of five patients in this series, suggests that this effect was determined by the associated bilateral subcaudate tractotomy.

Psychiatric diseases

Beneficial Effect of Subsequent Lesion Procedures Following Non-Response to Cingulotomy for OCD

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Introduction:

Cingulotomy is an effective therapy for appropriately selected patients with severe refractory OCD. However, optimal management for non-responders to cingulotomy remains unknown. We sought to determine whether a second lesion procedure offers therapeutic benefit after unsuccessful initial cingulotomy.

Methods:

We retrospectively studied 30 patients who were non-responders to cingulotomy within the first postoperative year. Full response was defined as $\geq 35\%$ decrease in YBOCS score, partial response as 25-34% decrease, and non-response as $< 25\%$ decrease. Change in YBOCS scores were compared between patients who underwent additional surgery (repeat cingulotomy or subcaudate tractotomy) and those who continued conventional therapy without additional surgery.

Results:

Following initial cingulotomy, 19 patients underwent a second lesion procedure, and 11 continued conventional therapy. Pre- and postoperative scores following initial cingulotomy did not differ between the two groups. At last follow up (51 months), mean YBOCS decrease was 43.6% in the surgery group and 13.1% in the conventional group ($p=0.009$). Furthermore, 10/19 in the surgery group were full and 4/19 were partial responders, while in the conventional therapy group only 2/11 were full and 2/11 were partial responders ($p=0.02$). There was no significant difference in outcome between repeat cingulotomy and subcaudate tractotomy.

Discussion:

Non-responders to initial cingulotomy for OCD who underwent a second lesion procedure had superior long-term responses than those who continued conventional therapy.

Conclusions:

Cingulotomy remains an effective option for patients with severe, treatment-refractory OCD. Non-responders to initial cingulotomy who are still appropriate surgical candidates should be considered for further surgical treatment.

Psychiatric diseases

Intraoperative capsular-nucleus accumbens boundary detection using MER during OCD DBS surgery

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Introduction. DBS (Lead 3387, Medtronic) targeting anterior limb of the internal capsule (ALIC) and nucleus accumbens (NAC) is effective in treating OCD. However, precise localization of the target is still problematic given that the scans used during surgery are not real-time. Brain shift following burr hole placement and dural opening is unpredictable and thus cannot be adjusted pre-operatively. Current report has shown that intraoperative real-time functional mapping of the boundary between ALIC and NAC can be achieved using low impedance MER (microelectrode recording) electrode.

Methods. A 19-yo male underwent bilateral DBS lead implant surgery targeting ALIC and NAC at 5 mm lateral, 0.9 mm anterior to the AC(AC-PC 13) and 5 mm inferior(AC-PC=24.2mm). A low impedance 0.3 M Ω microelectrode (BP-7 FHC Inc.) was employed during the recording following the planned trajectory using a 4-ch Leadpoint (Medtronic Inc.). Frequency histogram, RMS (root mean Square) and FFT above 200Hz were plotted real-time against depth.

Results. The recordings show the NAC boundaries on both sides and two 3387 leads were positioned to cover portions of the ALIC and NAC. Post-operative images confirmed the final lead positions were desired, and the patient has excellent efficacy.

Discussions. Larger tip electrodes (lower impedance) are sensitive in differentiating fiber from neuronal activities. Using this mapping data, stimulations of target produce efficacy with euphoric feelings.

Conclusions. Low impedance MER shown the capsule-NAC boundary in real time, and such a landmark was use for lead positioning. Both RMS and firing frequency are good in showing the capsule-nucleus interface.

Psychiatric diseases

Deep brain stimulation for the treatment of addiction: A survey of physicians and medical students

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Background: It is important to ascertain the knowledge and beliefs of those who may be involved in conducting trials of deep brain stimulation (DBS) for the treatment of addiction. Here, professional attitudes were assessed by surveying physicians and medical students at the University of Pennsylvania. **Methods:** Eleven individuals in the areas of neurology, neurosurgery, and psychiatry were consulted to identify areas to address in the survey. The IRB-approved survey was then administered to physicians experienced with DBS or addiction, as well as medical students with demonstrated interest in neuroscience. **Results:** Among an initial response sample of 20 physicians and 43 students, 75% of physicians and 42% of students thought DBS was safe to test in a clinical trial. Eighty percent of physicians and 65% of students agreed that investigating neurosurgical interventions such as DBS for addiction would be appropriate. Fifty percent of physicians and 26% of students expressed concern about financial compensation of research subjects in a clinical trial of DBS for addiction. Twenty percent of physicians and 15% of students were concerned that such investigation would cause a "slippery slope", in which the application of DBS may be inappropriately used in the future.

Discussion and Conclusion: This sampled group was largely supportive of the pursuit of a clinical trial to study the potential role of DBS in addiction management. However, this survey raised concerns for the implications of a positive trial on more broad applications of DBS and the role for financial compensation for research subjects in a trial.

Radiosurgery

Synchrotron-generated microradiosurgical hippocampal transections

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Introduction:

Synchrotron-generated microbeams are a novel tool to deliver high dose irradiation without significant dose spreading. Hippocampal microbeam transections have been performed in Wistar rats delivering an array of 25 micron beams with incident dose of 600 Gy .

Methods

Image-guided microbeam irradiation was performed on 12 healthy 3 weeks old Wistar rats (approximate weight 280 grams) . An incident dose of 600 Gy was delivered. Beam size was 25 micron. Follow-up included short and long-term behavioral and immunohistological assessments as well as high field MR imaging.

Results

The procedure was well tolerated. No behavioral abnormality was assessed over the following 9 months. Clear-cut microradiosurgical transections were identified within the hippocampus. Hippocampal neurogenesis was not affected. No evident MR abnormalities have been found

Discussion

This study shows that synchrotron-generated microradiosurgical hippocampal transections are a well tolerated .This approach can be useful to parcellize and disconnect an hippocampal epileptic focus.

Conclusions

Microbeam transections are associated with preservation of hippocampal architecture and neurogenesis. Microradiosurgical hippocampal transection are a novel tool of great interest to treat mesiotemporal epilepsy.

Radiosurgery

Frame-based versus frameless stereotactic radiosurgery: patient perceptions

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Introduction. We compared the perceptions of patients undergoing stereotactic radiosurgery (SRS) with and without the use of a stereotactic frame.

Methods. Patients undergoing SRS completed a questionnaire after treatment (n=91). There were 56 female (62%) and 35 male (38%) patients with a mean age of 61.9 years. Patients were placed into one of four groups, based on diagnosis and SRS method: benign with frame (BF), benign without frame (BFL), malignant with frame (MF), and malignant without frame (MFL). We compared patients'™ perceptions of discomfort, their willingness to have repeat treatment, and whether they would recommend SRS to others.

Results. Patients who perceived SRS to be uncomfortable included 90% for the BF group, 43.5% of the BFL group, 50% MF, and 30% MFL. When asked if they would repeat the SRS procedure if necessary, all patients in the MFL group would do so while 95.5% of BFL and 80% BF would, while only 75% in the MF group would do so. All patients in the BFL group would recommend the treatment to others, compared to 95.9% for MFL, 80% BF with only 62.5% of patients in the MF group. Frameless treatments approached statistical significance ($p = 0.05$) as a measure of favorable perception.

Discussion. Patients who undergo frameless radiosurgery perceive the procedure to be more tolerable than those having frame based SRS, and are more willing to repeat and recommend the treatment.

Conclusions. Avoidance of frame placement is more important than benign diagnosis in patients having a favorable perception of SRS.

Technology transfer

Development of chronically implantable electrochemical sensor for Wireless Instantaneous Neurotransm

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Introduction

Neurotransmitter release has become an important hypothesis for the mechanism of Deep Brain Stimulation (DBS), thereby raising the significance of measuring neurochemical release during DBS by such techniques as fast scan cyclic voltammetry (FSCV). Indeed, we have already obtained acute intra-operative human FSCV recordings during DBS neurosurgery using Mayo developed Wireless Instantaneous Neurotransmitter Concentration Sensor (WINCS) system. However, in order to perform such neurochemical monitoring on a chronic basis in the clinical setting, the conventional glass-capillary insulated microsensor needs improvements in safety, biocompatibility and longevity for FSCV recordings. Here, we present a novel design for a microsensor that is safe, biocompatible, and capable of recording neurochemical release chronically over a period of weeks in a large animal model.

Methods

The microsensor was fabricated from a carbon fiber sensor attached to a platinum extension wiring. The microsensors were stereotactically implanted with 3T MRI imaging guidance into the nucleus accumbens and the caudate of the pig. Simultaneous wireless FSCV and video recordings were performed in awake behaving animals every two days.

Results

The microsensors remained mechanically robust and electrochemically viable with a stable consistent background current, enabling WINCS recording for greater than two weeks. Analysis of the voltammogram demonstrated the successful measurement of adenosine.

Discussion and Conclusion

We successfully developed a microsensor that is suitable for chronic wireless FSCV recordings in awake behaving large animals. We feel that our novel chronic electrode may be utilized in the near future for monitoring neurotransmitter release evoked by DBS in humans on a chronic basis to assist in elucidating DBS mechanism.

Technology transfer

Development of Intraoperative CT with MRI Fusion for Functional Neurosurgery. A 3 year Experience.

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Introduction. Excellent target localization is crucial in neurosurgery. The ability to efficiently optimize location of implanted DBS leads or microelectrodes in a high-resolution MRI space would be a major advance. Intraoperative MRI is effective, but can be cumbersome, especially in proximity to electrophysiological recording equipment. Intraoperative CT (iCT) with preoperative MRI fusion is an attractive option. We review our experience between November 2008 and February 2012.

Methods. Volumetric low-resolution O-arm iCT images fused to preoperative MR scans (Medtronic Stealth) were used to assist intracranial surgery in 74 patients (45 male, 29 female; Age: 17-75 years). 62 patients had DBS lead implants (44 bilateral, 18 unilateral) for Parkinson's disease (46), cluster headaches (5), psychiatric disorders (4), dystonia (3), or tremor (4). Targets included the subthalamic nucleus, ventrolateral thalamus, internal pallidum, ventral striatum, subgenual cingulate and posterior hypothalamic areas. 12 patients had other intracranial procedures.

Results. DBS lead position was well-visualized intraoperatively in the preoperative MR image space. Image acquisition and fusion time was 15-30 minutes. With one automated fusion iteration a 3-5 mm error was often noted. 2 or 3 fusion iterations (mean 2.4) markedly improved error (<2mm). Lead location was adjusted in 35% of patients, mainly small changes within the same trajectory. Lead localization on O-arm iCT-MRI fusion compared to postoperative MRI was within 2 mm in most cases.

Discussion and Conclusion. O-arm iCT with preoperative MRI fusion can be applied to a wide variety of intracranial cases, provided brain shifts are limited. The technique is convenient and useful. Methodological pitfalls will be discussed.