Behavioral disorders

136: Tuesday, June 3, 2014, 11:06-11:16 am; PS #5

Use of the Human Connectome to Validate fMRI Changes in the Nucleus Accumbens Associated with Reward Cues during a Gambling Task

Ausaf A. Bari, Patrick Pezeshkian, Won Kim, Antonio DeSalles, Nader Pouratian
Los Angeles, CA

Introduction
The nucleus accumbens plays a central role in mediating reward and addiction. Based on its limbic connectivity, the nucleus accumbens is a logical candidate target for DBS for multiple neuropsychiatric disorders including addiction, obesity and depression. Here we use task-fMRI data mined from the Human Connectome Project to validate that activity in the nucleus accumbens changes in response reward cues during a gambling task.
Methods
Task and resting state fMRI data was obtained from 40 and 120 subjects respectively as described by the Human Connectome Project (http://humanconnectome.org). Task fMRI consisted of a gambling task as previously described by Delgado and Fiez. Group average task fMRI activity and resting state functional connectivity was processed and represented in grayordinate space as described by Woolrich and Van Essen.
Results
Group average task fMRI activity from 40 subjects revealed a significant increase in activity in the nucleus accumbens in the REWARD-PUNISHMENT contrast and a significant decrease in activity in the nucleus accumbens for the PUNISHMENT condition. In addition, resting state data from 120 subjects revealed signficant functional connectivity between the nucleus accumbens and the the anterior cingulate and medial prefrontal cortex.
Conclusions
Task fMRI data from subjects undergoing a gambling task show significant changes in activity in the nucleus accumbens associated with both reward and punishment. In addition, resting state fMRI data revealed significant functional connectivity between the nucleus accumbens and other limbic regions involved in reward processing such as the anterior cingulate and medial prefrontal cortex. The Human Connectome Project provides neurosurgeons with a robust data set to explore the correlation between behavior and functional and structural connectivity in order to confirm and identify candidate targets for DBS for various behavioral disorders.

137: Tuesday, June 3, 2014, 11:16-11:26 am; PS #5

Screening the Human Connectome for Potential DBS Targets for the Treatment of Drug Addiction

Ausaf A. Bari, Patrick Pezeshkian, Won Kim, Antonio DeSalles, Nader Pouratian
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Introduction
Drug addiction is currently one of the most devastating and costly disorders affecting humans. Successful and lasting treatment of drug addiction remains elusive and drug relapse remains a major problem. DBS of various limbic targets for the treatment of refractory drug addiction has been previously proposed by several groups. Here we describe data mining of structural and behavioral data from the Human Connectome Project to identify potential targets for DBS for the treatment of drug addiction.
Methods
We used the delayed discounting task as a surrogate for propensity towards addictive behavior and relapse. Delayed discounting data was summarized by 2 "area under the curve" (AUC) variables, AUC200 and AUC40000. Structural data consisted of volume, thickness and surface areas for 170 cortical and subcortical regions obtained from structural MRI scans of the same 223 subjects. Correlation between the AUC variables and structural parameters was calculated.
Results
Impulsivity as measured by the AUC for the delayed discounting task was significantly correlated with the following: right amygdala volume, left posterior middle frontal gyrus thickness, bilateral pars opercularis thickness, left frontal pole thickness, and right rostral anerior cingulate gyrus thickness ($r > 0.20$, $p < 0.01$, $n=223$).
Conclusions
These data suggest that several limbic as well as nonlimbic areas are significantly correlated with measures of impulsivity. These regions may underlie a propensity to addiction and/or relapse and should be investigated further as potential targets for DBS for drug addiction.

127: Monday, June 2, 2014, 1:30-1:40 pm; PS #4

Monitoring of Nerve Action Potentials (NAP) in Response to Transcranial Electrical Stimulation during Neurosurgical Procedures: A Pilot Study for Developing New Intraoperative Monitoring Technique

Alexander Ivanov, Ashley Selner, Faisal W. Waseem, John Fino, Guy Edelman, Konstantin V. Slavin, James L. Stone
Chicago, IL

Introduction
Transcranial Motor Evoked Potential (TcMEP) monitoring is a commonly used method to monitor corticospinal pathway integrity during neurosurgical procedures. The use of neuromuscular blocking (NMB) agents is not desirable during monitoring due to direct effect on muscle excitability. To this date, there is no available tool which could be used for motor pathway monitoring during complete NMB. In the past, we have been able to detect signals from the peripheral nerves after transcranial stimulation in patients who were completely pharmaceutically paralyzed. To explore the characteristics of these recorded potentials, we have launched a study where the feasibility of the transcranially evoked nerve action potentials (TcNAP) is investigated in a prospective cohort of 20 patients.
Methods
With proper IRB approval, the patients undergoing neurosurgical procedures who required TcMEP monitoring during the surgeries, were consented for the study. After anesthesia induction and complete muscle relaxation due to NMB agents, we began TcNAP monitoring. The primary outcomes measured were latencies and amplitudes of the TcNAP from ulnar and peroneal nerves and signal consistency. The intraoperative data was correlated with patient preoperative neurological status and co-morbidities; as well as with the basic characteristics of the TcMEP which were recorded after the surgery was started.
Results
By the time of this submission, five patients (2 male / 3 female, average age – 55 years) were enrolled into the study. Adequate TcNAP signal was obtained from one patient who did not have underlying co-morbidities and was neurologically intact prior to surgery.
None/poor/inconsistent NAP signals were recorded from the other 4 patients who had baseline myelopathy, diabetes, and obesity. The enrollment into the study (n=20) will be completed by the time of this presentation.
Conclusions
TcNAP monitoring may be a feasible alternative to TcMEP monitoring in selected patient population. Further prospective study is warranted to draw definite conclusions.

128: Monday, June 2, 2014, 1:40-1:50 pm; PS #4

Task Specific Interhemispheric Coupling in STN

Adam Olding Hebb, Sara Hanrahan, Joshua Nedrud, Soroush Niketeghad, Mohammad Mahoor, Jun Zhang, Felix Darvas
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Introduction
Cortical networks and quantitative measures of connectivity are of considerable interest in the study of brain function. A variety of methods quantify functional connectivity, and phase coherence measures direct synchronization between two cortical sites in a narrow frequency band. Despite the lack of direct anatomical connections between left and right STN, there is evidence for physiological connectivity. Here, we present our findings of phase synchrony and the causal interaction in STN between hemispheres in relation to a specific task, i.e. the movement of the left or right finger in patients suffering from PD.
Methods
We analyzed task specific phase synchronization and causality between left and right STN local field potentials (LFP) recorded from both hemispheres simultaneously during a cued movement task in four subjects with PD who underwent DBS surgery. We used a data driven approach to determine inter-hemispheric channel pairs and frequencies with a task specific increase in phase locking.
Results
We found significant phase locking between hemispheres in the alpha frequency (8-12 Hz) in all subjects concurrent with finger movement, but not dependent on which side was moved. In all subjects, phase synchronization increased over baseline at or prior to movement onset and lasted throughout the motion. Left and right movement showed similar activation patterns. Granger causality at the phase-locking frequencies between synchronized electrodes revealed a unilateral causality from right to left STN regardless of which side was moved.
Conclusions
Phase synchronization across hemispheres between basal ganglia structures supports the existence of a bilaterally connected network with lateralized regions of specialization for motor processing, and our results suggest that a simple unilateral motor program activates this bilateral network. Understanding phase synchronization in natural brain functions will be critical for the development of next generation DBS systems that aim to either minimize the negative impact on these functions, or augment these functions.

129: Monday, June 2, 2014, 1:50-2:00 pm; PS #4

The Development of High-Performance Communication Neural Prostheses

Paul Nuyujukian, Vikash Gilja, Jonathan C. Kao, Joline M. Fan, Sergey D. Stavisky, Stephen In-Sun Ryu, Krishna V. Shenoy
Stanford, CA, and Palo Alto, CA

Introduction

Neural prostheses, or brain-machine interfaces, are an emerging class of medical systems designed to restore lost function to those suffering from paralysis, be it from injury or degenerative disease. Systems can range from communication prostheses that control computer cursors and keyboards to motor prostheses that manipulate robotic arms and wheelchairs. Over the last several years, gains in performance and reliability of these systems have been largely through algorithmic and system-level innovation of intracortical electrode array based systems.

Methods

We implanted two rhesus macaques with 96 channel Utah electrode arrays in motor regions of cortex (M1 and PMd) and trained them to make point-to-point reaches to navigate a cursor in a virtual world. We implemented a neural prosthesis using an algorithm we developed (ReFIT-KF) to control the cursor, resulting in more accurate and reliable cursor control versus conventional algorithms. Additionally, a hidden Markov model (HMM) was later run in parallel to the cursor control algorithm, enabling a "click" selection signal to be detected. System performance was measured via real-world metrics of achieved bitrate and typing speed (words per minute). System reliability was measured both by sustained performance within a day's session and across days, both with and without prosthesis recalibration.

Results

This system achieved bitrates of 4 bits per second (bps) and a typing rate of 10 words per minute (wpm) using a cursor driven solely by neural activity. When paired with the HMM, it achieved up to 6 bps and 15 wpm. Performance was reliable for hours across daily sessions. Furthermore, in one monkey, the prosthesis was stable for nearly two years without recalibration.

Conclusions

By improving communication neural prostheses from an algorithmic and systems perspective, we have significantly increased the performance and reliability of such systems, bringing them closer to clinically relevant translation.

130: Monday, June 2, 2014, 2:00-2:10 pm; PS #4

High Performance Communication Using Neuronal Ensemble Recordings from the Motor Cortex of a Person with ALS

Chethan Pandarinath, Vikash Gilja, Christine Blabe, Beata Jarosiewicz, Janos A. Perge, Leigh R. Hochberg, Krishna V. Shenoy, Jaimie M. Henderson
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Introduction

Brain-Machine Interface (BMI) systems have the potential to restore communication, mobility, and independence for persons with paralysis, by translating neural activity into control signals for assistive devices. Recent demonstrations with non-human primates (NHPs) showed that BMIs using chronically implanted intracortical electrodes can achieve high-performance control of computer cursors; thus these systems could provide a rapid method of communication for persons with paralysis. Here we demonstrate the successful translation of one such system to a human research participant, yielding a high-performance communication interface used by a person with Amyotrophic Lateral Sclerosis (ALS).

Methods

A 50-year-old woman with ALS underwent implantation of an array of 100 silicon microelectrodes into the “hand knob” area of the precentral gyrus, as part of a multi-site pilot clinical trial (Braingate2, IDE). During weekly experimental sessions (2-3 days/week), the participant guided a computer cursor under neural control to acquire targets on a computer screen. Using a blinded study design, we compared the performance of the previous state-of-the-art algorithm (Velocity Kalman Filter, VKF) against a novel control algorithm developed through NHP research, “ReFIT”. After each experimental block, the participant subjectively rated its ease-of-use on a Visual Analog Scale (VAS). Finally, she used the BMI to communicate by controlling a standard assistive typing program.

Results

BMI control using the novel algorithm (ReFIT) showed a 20% increase in performance over the previous state-of-the-art algorithm in an 8-target acquisition task (1 sec/target vs. 1.2 sec/target, $p<0.01$). Further, the participant’s self-report described a near doubling in ease of use (2.3 vs. 4.2 on the VAS, $p<0.01$). Finally, using the novel algorithm, the participant was able to comfortably communicate at ~6 words-per-minute in a free-paced typing task.

Conclusions

BMIs based on recent algorithmic advances, such as ReFIT, can provide high-performance communication options, which would substantially improve quality of life for persons with paralysis.

131: Monday, June 2, 2014, 3:30-3:40 pm; PS #4

Intraspinal Microstimulation using MINCS to Evoke Hind Limb Movements in a Porcine Model of Spinal Stimulation

Peter J. Grahn, Grant William Mallory, Juho Jeong, Jan T. Hachmann, Darlene Angela Lobel, Allan J. Bieber, Kevin Bennet, Kendall H. Lee, J. Luis Lujan
Rochester, MN

Introduction
Functional electrical stimulation (FES) techniques employed during acute spinal cord injury (SCI) rehabilitation have been shown to enhance neurorecovery. Intraspinal microstimulation (ISMS) is an emerging FES technique that holds promise to overcome some of the limitations facing current FES devices. ISMS is thought to work by directly activating alpha motor neurons via electrical excitation delivered through microelectrodes implanted within the ventral horn gray matter of the spinal cord. Here, we describe the use a novel investigational FES device, Mayo Investigational Neuromodulation Control System (MINCS), in a pig model of ISMS to develop a map of the lumbar spinal cord motor circuitry for efficiently targeting and evoking desired limb functions.
Methods
The lumbar spine was exposed from the L2 to L5 vertebra in five porcine animals and ISMS electrodes were implanted at various locations within the lumbar spinal enlargement to evoke hind limb movements. The spinal cord was systematically stimulated, via wireless control of MINCS, at 50 Hz using 200 µs stimuli. Pulse amplitude was systematically increased from 50 to 300 µA, in 20 µA increments. Electromyographic and kinematic recordings were obtained from the major muscle groups and kinematic markers were placed on the joints of the hind limbs.
Results
MINCS was successful in controlling hind limb movements of the anesthetized pig. Stimulation at the L3 vertebral level produced hind limb flexion responses along with hip adduction. At the L4 vertebral level, minimal responses were observed. Furthermore, stimulation at the L5 vertebral level evoked strong hind limb extension combined with hip abduction.
Conclusions
Development of a map of the lumbar spinal cord motor circuitry in the pig model of spinal stimulation will provide efficient electrode targeting for evoking desired limb functions. These results suggest ISMS may be able to allow specific limb movements for walking and weight-bearing standing.

132: Monday, June 2, 2014, 3:40-3:50 pm; PS #4

Optogenetic Inhibition Using a Genetically Encoded Bioluminescent Light Source

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Introduction
The use of optogenetics in vivo faces many important challenges that limit conducting chronic studies and translation of optogenetic approaches into a clinically meaningful context. Several relate to the light source, which currently relies on using lasers or LEDs coupled to optical fibers implanted into the brain. These light sources are impractical to use in long term in vivo settings (e.g. hardware dependency, have limited tissue penetrance) and also pose a significant safety risk (e.g. tissue damage, heat-induced injury). The overall goal of this project is to address the current technical limitations of using optogenetics in vivo by developing bioluminescent proteins as an alternative light source for activating light-sensitive opsins.
Methods
We developed various novel optogenetic constructs encoding opsin and luciferase proteins and have delivered them to HEK293 cells and dissociated cortical neuron cultures. Renilla luciferase and Halorhodopsin were either delivered separately or together as a fusion protein using viral vectors. Electrophysiological responses to bioluminescence were determined with whole-cell intracellular recordings.
Results
We demonstrate a valid proof-of-principle showing that a red-shifted Renilla luciferase can activate Halorhodopsin in vitro. Transfected HEK293 cells emitted bioluminescence upon addition of coelenterazine, resulting in concomitant hyperpolarization of membrane potential and outward flow of current. Transduced cortical neurons similarly emitted bioluminescence upon addition of coelenterazine, resulting in attenuation of neuronal firing. These cells also responded robustly to illumination with external light. Such effects were never seen in non-transfected cells. Experiments are currently underway with cortical neurons grown on multielectrode arrays to assess the modulatory effect of this approach on network activity. Acute brain slice and in vivo experiments are also being launched.
Conclusions
We have shown that the use of bioluminescent proteins offers an alternative means to activating light-sensitive opsins in a purely hardware-independent manner, adding to the versatility of the optogenetic approach for neuromodulatory applications.

133: Monday, June 2, 2014, 3:50-4:00 pm; PS #4

Novel Percutaneous Scalp Mount Base for SmartFrame® Enables Minimally Invasive MR-Guided Stereotactic Laser Ablation and DBS Electrode Placement

David Lozada, Jon T. Willie, Robert E. Gross
Atlanta, GA

Introduction
An expendable skull-mounted MR guidance miniframe (ClearPoint® SmartFrame®) has been optimized for DBS surgery. However, the original device disadvantageously requires a large incision and burr hole, which is not optimal for minimally invasive approaches. A recently modified scalp mounted frame base was designed for percutaneous skull fixation, accommodating minimal incisions and twist drill hole access. We report our experience with this device modification for multiple stereotactic applications.
Methods
We utilized the scalp mounted frame base and SmartFrame® tower to perform 23 MR-guided procedures, including 18 stereotactic laser ablations (SLA) for epilepsy and 5 GPi-DBS electrode placements for movement disorders. Approaches were either occipital (SLA, n=15) or frontal (SLA, n=3; DBS, n=5). Stereotactic accuracy, hospital length of stay, and complications were measured.
Results
The scalp-mounted frame facilitated minimal or stab incisions. For occipital and frontal approaches, mean 2D radial errors were 2.2 ± 0.3 mm and 1.3 ± 0.28 mm, respectively. For SLA and DBS indications, 2D radial errors were 2.16 ± 0.26 mm and 0.9 ± 0.22 mm, respectively. The median hospitalization for the group was 1 day. There were no surgical site complications, but one patient sustained a left occipital intraparenchymal tract hemorrhage causing transient nonoperative right superior quadrantanopsia.
Conclusions
The scalp-mounted modified SmartFrame® accommodates minimally invasive MR-guided stereotactic neurosurgical procedures while maintaining safety and accuracy.

134: Monday, June 2, 2014, 4:00-4:10 pm; PS #4

Stereotactic Integration of 3D Photographic Texture-encoded Stereovision Surfaces

David W. Roberts, Xiaoyao Fan, Songbai Ji, Alex Hartov, Keith Paulsen
Lebanon, NH

Introduction
Photographic visualization and documentation of the operative field is a well recognized, powerful adjunct to radiological diagnosis and surgical intervention. Two-dimensional photographs and video have been co-registered with MRI, but incorporation of actual three-dimensional visual images into stereotactic space enables full integration of this optical information into three-dimensional multimodality databases.
Methods
A stereoptic-based system compromised of two 1024 X 768 color CCD cameras attached to an operating microscope at a binocular port and employing an optical flow algorithm has been further developed to provide 3-D coordinate localization of each pixel at a frame rate of 15/sec. Accuracy of the current implementation of this system was assessed during surgery by feature localization relative to a tracked stylus. Surgical field localization with respect to preoperative MRI, coordination of functional mapping, displacement mapping of cortical features and implanted electrodes, and intraoperatively updated registration were performed with this system and their utilities assessed.
Results
Accuracy assessment by feature localization relative to a tracked stylus was 1.0 ± 0.5 mm. Application in 150 epilepsy and tumor cases superposed high resolution, surface-contour color images on MRI 3-D reconstructions in either static or interactive display. In 32 epilepsy cases these were used for intraoperative planning, localization, guidance, and documentation. Displacement fields enabled intraoperative updated registration from initial errors of 4.0 - 9.8 mm.
Conclusions
Valuable, high resolution optical information in the form of 3D photographic texture-encoded stereovision surfaces can be efficiently acquired and readily accessed for such utilities as co-registration, deformation mapping, updated registration, correlation, and optical imaging. Not least, this methodology provides archival documentation of the surgical procedure in the same coordinate space as traditional neuroimaging.

135: Tuesday, June 3, 2014, 10:51-11:06 am; PS #5

A Phase II Dose Escalation Study of Cervical Targeted Intraspinal Microinjection in ALS: Interim Peri-operative Morbidity and Peri-procedural Outcomes

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Atlanta, GA, and Ann Arbor, MI

Introduction
Six cervical microinjection procedures have been completed in the first Phase II US trial assessing a stem cell-based treatment for Amyotrophic Lateral Sclerosis. This trial utilizes a dose escalation paradigm in early stage ambulatory patients. This study follows completion of a Phase I trial that demonstrated the safety of unilateral cervical plus bilateral thoracolumbar microinjection series in ambulatory ALS patients.
Methods
Fifteen patients are planned to receive eighteen microinjection procedures over a total of five cohorts (n=3/cohort) in a multi-center trial to complete enrollment in May 2014. Six cervical microinjection procedures (e.g. Emory University (n=3), Massachusetts General Hospital, University of Michigan (n=3)) have been completed. A previously described microinjection platform and floating cannula system have delivered ventral-horn targeted cellular graft injections at the C3-5 level. NSI-566RSC [$2x10^4$ cells/µL] was delivered through either 10 injections (5/side; Group-A) or 20 injections (10/side; Group-B). All patients received a 10µl graft with rostrocadual spacing of 4 mm and delivery 1-2 mm medial to the dorsal root entry zone. This resulted in a cumulative dose of either $2x10^6$ cells or $4x10^6$ cells. Triple agent immunosuppression regimen was administered. Detailed neurologic outcomes were recorded.
Results
Length of stay ranged from 5-10days (mean – 6). Operative time has ranged from 254-353min (mean – 298 min). One patient received instrumentation secondary to pre-operative loss of cervical lordosis. One episode of mild tract hemorrhage was recorded. No change in neuromonitoring was noted. No serious adverse events have been reported. Incisional pain is the most commonly reported post-surgical adverse event attributed to the procedure.
Conclusions
These preliminary findings extend the safety results from our recently completed Phase I trial. The current trial seeks to establish a maximum tolerated dose for the delivery of biologic payloads to the vulnerable ALS spinal cord. This data supports the cervical spinal cord to be able to tolerate a payload of $4x10^6$ cells and up to twenty associated cord penetrations.

200 – Poster presentation

The development of a closed loop controller for deep brain stimulation in porcine model: toward smart neuromodulation

Grant William Mallory, Peter J. Grahn, Inyong Kim, Seungleal Paek, Allan J. Bieber, Su-Youne Chang, Kevin Bennet, Kendall H. Lee
Rochester, MN

Introduction
Deep brain stimulation (DBS) is effective therapy for a variety of neurologic and psychiatric disorders. However, outcomes largely depend on the ability to determine optimal stimulation parameters via trial-and-error methods. Improper settings can result in adverse effects, early battery depletion, and ultimately, treatment failures. Thus, there is an impetus for novel and advanced DBS systems that utilize the brain's dynamic environment to smartly guide neuromodulation. We hypothesize that fast-scan cyclic voltammetry (FSCV) measurements of evoked neurotransmitter level may be used as feedback signal to control stimulation parameters during DBS.
Methods
Using a porcine model, we characterized striatal dopamine release evoked with varying DBS parameters (pulse width, frequency, and voltage). FSCV was performed with chronic carbon-fiber microelectrodes (CFM) and a wireless instantaneous neurotransmitter concentration sensor (WINCS). Stimulation was delivered via a human DBS electrode (Medtronic 3389) implanted in the substantia nigra / ventral tegmental area and subthalamic nucleus (STN) coupled to MINCS (Mayo Investigational Neuromodulation Control System).
Results
Electrical stimulation elicited a stimulus time-locked increase in striatal dopamine release that was stimulus dependent. Increasing pulse width and frequency, demonstrated a linear increase in dopamine release, whereas voltage-dependent increases in evoked dopamine release exhibited a sigmoidal pattern attaining a plateau between 5 and 7V of stimulation.
Conclusions
Our results indicate that dopamine release evoked by DBS may be precisely controlled by varying stimulation parameters of PW, frequency, and voltage. These results suggest the exciting possibility that computational modeling can be used to parameterize relationships between extracellular dopamine and that these models can further be used to dynamically predict stimulation parameters as a function of target dopamine levels. We envision such a system to allow an electrochemical smart feedback neuromodulation system in the future that may be used to treat neuropsychiatric disorders.

202 – Poster presentation

Stereotactic Striatal Injection of a Regulated Viral GDNF Expression System in Non-human Primates

Seth Franklin Oliveria, Kelly D. Foote, Ronald Mandel
Gainesville, FL

Introduction

Glial derived neurotrophic factor (GDNF) is a trophic factor for dopaminergic (DA) neurons, which is neuroprotective for DA neurons in animal models. GDNF is considered a potential treatment of Parkinson's disease to slow disease progression. However, initial trials of direct delivery of GDNF protein to the brain for PD failed to generate positive clinical results. This lack of observed clinical efficacy is most probably due to an unsuccessful delivery method rather than a failure of GDNF activity. We have thus developed a doxycycline-regulated viral vector capable of expressing more homogeneous levels of GDNF, which demonstrates therapeutic benefit in rodent models of PD. We tested the safety and efficacy of striatal vector injection in primates as a precursor to potential human trials.

Methods

We performed bilateral stereotactic viral vector injections into the anterior putamen of six cynomolgus macaques. Each animal received both constitutively active and regulated vectors in separate hemispheres. Half of the animals received oral doxycycline after injection. After a 21-day incubation period animals were sacrificed to permit tissue analysis, including quantitation of GDNF expression using LiCor Odyssey infrared imaging.

Results

All animals had widespread, robust GDNF expression in the hemisphere receiving constitutively active vector. More focused GDNF expression was observed at the site of injection in the hemisphere receiving regulated vector. No GDNF was observed in animals treated with doxycycline. The relative level of GDNF expression by the doxycycline-responsive vector compared to the constitutively active vector is similar to that observed in rodents. No significant adverse events were observed.

Conclusions

In primates, striatal transduction of a drug-responsive GDNF expression system results in focused GDNF production that can be controlled with doxycycline. The results of this pilot study indicate that this regulated viral GDNF expression system is appropriate for further preclinical testing in primate models of PD, and potentially human clinical trials.

203 – Poster presentation

Super-selective Amygdalohippocampectomy in Patients Treated by Laser Ablation

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Jacksonville, FL

Introduction

Retention of the mesial structures is responsible for surgical failures in patients with drug-resistant mesial temporal lobe epilepsy (MTLE) due to mesial temporal sclerosis (MTS). Stereotactic laser ablation allows precise obliteration of the amygdalohippocampal complex (AHC). Utilization of real-time brain MRI permits immediate information about the region of ablation. We report clinical outcomes in a cohort of patients with MTS who received laser ablation of AHC as well as changes in the volume of AHC on pre- and post-operative MRI.

Methods

Eleven patients underwent pre-surgical evaluation for drug-resistant focal seizures. A 3-T brain MRI demonstrated abnormality in 10/11 patients. One patient with normal MRI had seizures coming from left mesial temporal lobe recorded by depth electrodes. Occipital-temporal laser ablation was performed in all patients as part of an IRB approved study protocol. Post-operative AHC ablation was compared with the pre-operative MRI.

Results

Eleven patients (5F: 20-68 years) with MTLE received laser ablation after multi-disciplinary evaluation. A 3-month post-operative MRI was obtained in 9 patients. More than 75% of the amygdala and 100% of the head-to-tail hippocampal region was ablated in 9/11 patients. One patient had < 25% of parahippocampal gyrus and the uncal recess ablated. One patient had 50% of the parahippocampal gyurs and the anterior-medial hippocampus ablated with a greater T2 signal in the remaining AH. Two patients experienced a single post-operative seizure (complete ablation) and 10/11 remain seizure free. One patient had the relapse of seizures after 4 months of seizure-free period. One patient experienced right quadrantanopia post-operatively.

Conclusions

Minimally invasive laser ablation allows for selective targeting of AHC with a near perfect anatomic amygdalohippocampectomy. Even in cases of incomplete ablation, early seizure freedom was obtainable due to the interruption of seizure network. Ongoing data collection is being performed to evaluate long-term efficacy of this novel technique.

204 – Poster presentation

Lateral Cerebellar Nucleus Activity of the Ischemic Rat During a Reaching Task

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Introduction
Stimulation of the lateral cerebellar nucleus (LCN) at beta band frequencies has been shown to improve post-stroke reaching performance of the rodent. We hypothesize that stimulation delivered in a way that mimics the intrinsic modulation of the LCN may further promote neurorehabilitation. To that end, we recorded the oscillatory modulation of the rodent LCN during the performance of a skilled reaching task in the naïve and stroked rat.
Methods
Rats were implanted with five-electrode, high-impedance arrays into the LCN. Following recovery, animals were trained to perform a food pellet reaching task with the paw ipsilateral to the implanted electrode array. A small stroke was then produced over the motor cortex corresponding to the paw used for reaching. Training on the pellet-reaching task was resumed after a recovery period. The performance of the task was videotaped to allow for reaching attempts to be classified into failed (MISSES) or successful (HITS). Local-field activity was recorded wirelessly from each electrode while the rodent performed the reaching task.
Results
Preliminary results from animals before and after stroke indicate that there is a shift from lower frequencies of beta band to high beta when comparing the HITS vs. MISSES of a naïve rat. In contrast, the stroked rat shows a shift to high beta during HITS trials. This beta activity is markedly absent during stroked rat MISSES, with a high power gamma band present during movement.
Conclusions
We demonstrate differences in frequency band modulation between the stroked and naïve rat during a skilled reaching task. Future experimentation will examine whether stimulation at the intrinsic pattern of the LCN enhances recovery following stroke.

205 – Poster presentation

An Automated Targeting System for Subthalamic Nucleus Deep Brain Stimulation

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Introduction
Accurate surgical placement of electrodes is critical to the success of deep brain stimulation (DBS) of the subthalamic nucleus (STN) for Parkinson disease. Suboptimal targeting in STN DBS surgery may arise from poor initial target localization, frame-based targeting error, or intraoperative brain shift. These uncertainties can make STN DBS surgery a challenging procedure, particularly for non-specialty trained neurosurgeons.We have developed an automated method to guide STN DBS electrode localization, more accurately identifying the trajectory of intraoperative microelectrode recording (MER) on magnetic resonance (MR) images during DBS surgery.
Methods
Our computerized method is based upon the relationship between the high-frequency band signal (HFB, 500-2000 Hz) from MER and voxel intensity on MR images. The HFB profile along an MER trajectory recorded during surgery is compared to voxel intensity profiles along 100,000 potential trajectories in the region of the surgically planned trajectory. From these comparisons of HFB recordings and potential trajectories, an estimated MER trajectory is calculated. This calculated trajectory is then compared to the actual trajectory, as estimated by post-operative high-resolution computed tomography (CT).
Results
We compared 20 planned, calculated, and actual trajectories in 13 patients who underwent STN DBS surgery at our institution. Targeting errors for our calculated to actual trajectory (2.33mm ± 0.2mm) were significantly less than errors for the surgically planned to actual trajectory (2.83mm ± 0.2mm, $P = 0.01$), improving targeting accuracy in 70% of individual cases (14/20). Moreover, in 4 of 4 initial MER trajectories that missed the STN, our method accurately indicated the required direction of targeting adjustment for the DBS lead to intersect the STN.
Conclusions
An automated, computer-based algorithm simultaneously utilizing MER and MR information may potentially improve intraoperative localization during STN DBS surgery.

206 – Poster presentation

Optogenetic Activation of Neurons in Swine

Su Youne Chang, Allan J. Bieber, Inyong Kim, Paul Hoon-Ki Min, Erika K. Ross, Seungleal Paek, Michael P. Marsh, Kevin Bennet, Kendall H. Lee
Rochester, MN

Introduction

Optogenetics combines genetic and optical techniques to control the electrical excitability of targeted cells in freely behaving animals. Because of its high specificity and selectivity, optogenetic approaches have been used extensively to investigate the functions of specific brain circuitry. Optogenetic techniques have been widely used in rodents, and recently an optogenetic tool box was published for non-human primates; however, its application has been limited in other large animal species. Our research team has developed a large animal model (swine) for translational research. The swine model is increasingly being used in the field of neuroscience because the anatomy and size of the swine brain is very comparable to that of non-human primates. In this study, we used electrophysiology and electrochemistry techniques to test the efficacy of currently available optogenetic tools in swine.

Methods

To identify the target for virus injection and optic fiber implantation, a preoperative anatomical MRI was obtained in a 3T MR scanner. After confirmation of the target coordinates in the ventral tegmental area (VTA) and substantia nigra pars compacta (SNpc), optogenetic AAV vectors (AAV-ChR2-CaMKII) were injected through a burr hole in the skull with a Hamilton syringe (24 Ga needle). Five to seven weeks after injection, electrophysiological monitoring in the VTA/SNpc area was used to assess neuronal activation following 460nm LED stimulation to activate ChR2. Electrochemical recording was also performed to characterize optical stimulation evoked dopamine release.

Results

AAV-ChR2-CaMKII was expressed in the VTA/SNpc in swine. Optical stimulation generated robust action potentials and evoked dopamine release in a stimulation time-locked manner.

Conclusions

We successfully demonstrated the feasibility and functionality of optogenetics as an experimental strategy in swine. The successful application of optogenetics will add a new dimension to the swine model as a tool for neuroscience research and as a model for the study of functional brain circuitry.

115: Monday, June 2, 2014, 10:00-10:10 am; GS #2
An Automated Technique for the Quantification of Cortical Susceptibility to After Discharges

Tyler Davis, Paul A. House, F. Edward Dudek
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Introduction
Accurate and efficient identification of the seizure onset zone (SOZ) is a crucial step in determining the likelihood of surgical cure in the care of patients with partial onset, medically refractory epilepsy. To identify the SOZ, patients traditionally undergo intracranial electrocorticographic monitoring (iECoG) where antiepileptic medications are reduced until spontaneous seizures are recorded. The SOZ is then subjectively determined by trained experts. Although this approach is the "gold standard", it is costly, time-consuming, and imperfect. Stimulation mapping to identify areas of critical cortical function is routinely employed during iECoG monitoring. Stimulation mapping can also inadvertently trigger afterdischarges. Areas of cortex that are susceptible to these stimulation-induced responses have been related to the SOZ. Current techniques to quantify afterdischarges, however, are labor intensive and, as such, are typically used in a post-hoc fashion.
Methods
We have developed an automated and unbiased statistical approach to quantify afterdischarges. Using data from standard stimulation mapping routines, afterdischarges are automatically detected by identifying significant changes in spectral power from 10 to 80 Hz for one second intervals immediately before and after stimulation events. The percentage of significant events is then calculated for each electrode and is used to create maps of cortical susceptibility to afterdischarges and to estimate the SOZ.
Results
This approach has been tested on data from several patients, and the results have been compared to the clinically-determined SOZ. Average specificity and sensitivity values demonstrate agreement between the estimated and clinical zones.
Conclusions
We present the development and implementation of this automated approach. The speed and reproducibility of this approach may allow for the incorporation of cortical susceptibility to afterdischarges into clinical decision-making.

116: Monday, June 2, 2014, 10:10-10:20 am; GS #2
Lateralization of Temporal Lobe Epilepsy by Imaging-Based Response-Driven Multinomial Multivariate Models

Jason M. Schwalb, Mohammad-Reza Nazem-Zadeh, Hassan Bagher-Ebadian, Fariborz Mahmoudi, Hamid Soltanian-Zadeh
Detroit, MI

Introduction
Multiple modalities are used in determining laterality in temporal lobe epilepsy. It is unclear how much different imaging modalities should be weighted in decision-making.
Methods
Volumetrics, mean and standard deviation of FLAIR intensity, and mean of normalized ictal-interictal SPECT intensity on left and right hippocampi were extracted from preoperative images of forty-five retrospective TLE patients with surgical outcome of Engel class I. Using multinomial logistic function regression, the parameters of various univariate and multivariate models were estimated.
Results
Among univariate response models, for the response model with mean SPECT attributes the lowest fit deviance was 65.1±0.1. A false alarm probability of 0 and 0.04 for the left and right epileptogenic sides were achieved respectively. However, the response model with mean FLAIR attributes resulted in highest probability of detection 0.93 and 0.94 for left and right epileptogenic sides, respectively. The multivariate response model with incorporating all attributes of volumetrics, mean and standard deviation FLAIR, and mean SPECT intensity, reached to a significantly lower fit deviance than for other response models (12.3±0.1, $p < 0.001$). It reached probability of detection of 1 with no false alarms. We were able to correctly lateralize the fifteen TLE patients who had undergone phase II intracranial monitoring. Therefore, phase II intracranial monitoring might have been avoided for this set of patients. Based on this lateralization response model, the side of epileptogenicity was also detected for all thirty patients who had proceeded to resection with only phase I of EEG monitoring
Conclusions
The proposed multinomial multivariate response-driven model for lateralization of epileptogenicity in TLE patients can help in decision-making prior to the surgical resection and may reduce the need for implantation of intracranial monitoring electrodes.

117: Monday, June 2, 2014, 10:20-10:30 am; GS #2

Outcomes of Stereotactic Laser Ablation for Treatment- Resistant Epilepsy in the Pediatric Population with 1 year follow-up

Daniel Curry, Anil Shetty, Angus A. Wilfong
Houston, TX

Introduction
Approximately 7600 new cases of pediatric epilepsy occur each year and it is estimated that at least one-third of them with be refractory to medical management. Pediatric epilepsy surgery is vastly underutilized (~400 /year) due to its invasiveness and morbidity. Stereotactic laser ablation (SLA) is a minimally invasive alternative for surgical candidates. We present the safety and patient outcomes in twenty patients.
Methods
Twenty patients with medically intractable lesional epilepsy, ages 2-18, underwent an IRB-approved focus ablation. Epileptic foci had varied etiologies (HH:12,FCDs:4,MTS:3,TS:1). An FDA-cleared surgical laser ablation system (Visualase Thermal Therapy System; Visualase, Inc., Houston, TX) was employed in this work. The cooled laser applicator (1.6 mm in diameter) includes a fiberoptic applicator with either a 1 cm or a 3 mm light-diffusing tip. Framed stereotaxy was used to target the lesion and MR Thermography was utilized. After a test dose of 3-4 W confirmed applicator position, doses of 5-12 W for 45-120 seconds were used to ablate the foci. Safety limits (50°C) were placed near the margin of the desired thermal ablation zone to protect critical structure. Post-ablation DWI, T1-weighted plus gadolinium contrast (T1 + Gd), and FFE series were acquired. Follow-up period was from 11-41 months.
Results
13 patients were seizure free after one ablation, 3 after a second procedure. In the 19 pts with > 1 year follow-up, 11 achieved Engel 1 status. 6 patients underwent repeat procedures, three ablations and three craniotomies. Complications included 3 transient short term memory dysfunctions, one sub-clinical subarachnoid hemorrhage, and one CSF leak. Average LOS was 1 day.
Conclusions
Stereotactic laser ablation (SLA) for epileptic foci has demonstrated rates of seizure freedom that match / are comparable to open surgical results. Low morbidity, reduced LOS and ability to stage procedures, along with the safety of real-time MR guided ablation are advantages.

118: Monday, June 2, 2014, 10:30-10:40 am; GS #2

Modulation of Hippocampal Neural Activity via Optogenetic Stimulation of the Medial Septum

Nealen Laxpati, Megha Chiruvella, Jack Tung, Claire-Anne Gutekunst, Robert E. Gross
Atlanta, GA

Introduction
The medial septum is a pacemaker of the hippocampal theta rhythm, which in turn is associated with the prevention or cessation of epileptic activity. Modulating hippocampal theta could therefore prove effective for seizure control. There are three unique populations within the medial septum – glutamatergic, GABAergic, and cholinergic neurons. We hypothesize that medial septal GABAergic and glutamatergic neurons pace hippocampal oscillatory activity, whereas cholinergic neurons provide muscarinic control over theta power.
Methods
Sprague-Dawley and Long-Evans rats were injected in the medial septum with AAV viruses encoding ChR2 (excitatory) or eNpHR3.0 (inhibitory) channels in glutamatergic (CaMKIIa), GABAergic (hSyn), or cholingergic (EF1a-DIO, transgenic) neurons. An optical fiber was implanted in the medial septum alongside a 16-channel microwire multielectrode array recording from hippocampal layers CA1 and CA3. Animals underwent LED stimulation across frequencies from 5-42 Hz and pulse widths of 1-50 ms. Recorded electrophysiological data was spectrographically analyzed using custom-written Matlab scripts.
Results
Optogenetic excitation and inhibition of medial septum subpopulations altered hippocampal neural activity. In non-epileptic animals increases in stimulus frequency-specific power in the hippocampal local field potential were observed with hSyn- and CaMKIIa-ChR2, but not in ChAT-ChR2 or controls. CaMKIIa-ChR2 and hSyn-ChR2 rats could phase-lock extant hippocampal theta oscillations to the optical stimulus as well. Hippocampal single-unit activity was modulated in hSyn and ChAT-ChR2 animals, but was unaffected by CaMKIIa-ChR2 stimulation. Inhibition of hSyn-eNpHR3.0 animals produced a frequency specific response not seen in CaMKIIa animals.
Conclusions
We used cell-type specific optogenetic stimulation and multielectrode recording to functionally dissect the neural circuitry of the septohippocampal axis. Our results indicate that while GABAergic and glutamatergic neurons of the medial septum can control hippocampal theta oscillations, cholinergic neurons of the medial septum are not pacing theta. This suggests that these neurons play some other role, perhaps in synchrony with input from the other populations.

124: Monday, June 2, 2014, 4:25-4:35 pm; PS #3

The Effects of DBS at Multiple Targets on Network Activity within the Papez Circuit

Paul Stypulkowski, Scott Stanslaski, Timothy Denison, Jonathon Giftakis
Minneapolis, MN

Introduction

The opportunity to investigate the effects of deep brain stimulation on neural networks has recently been expanded by the development of implantable systems that allow for neural recordings in conjunction with therapeutic DBS. We previously reported on the initial evaluation of these devices in a chronic large animal (ovine) model, and here extend those studies to examine DBS applied at different nodes within Circuit of Papez. Specifically, we have compared the effects of DBS in the following targets: anterior thalamus, fornix, and hippocampus, all targets which are under clinical investigation for the treatment of disorders such as epilepsy and Alzheimer's disease.

Methods

Following anesthesia and 1.5T MRI acquisition, leads were implanted in the hippocampus and anterior thalamus (n=3) or fornix (n=1) in four animals using a frameless stereotactic system, and connected to modified neurostimulators (Activa PC&S). Chronic, awake recordings of evoked potentials (EPs) and local field potentials (LFPs) in response to DBS at these different network nodes were collected with the implanted device and analyzed off-line.

Results

Evoked potentials could be elicited within the Papez circuit by stimulation at each of the three different targets, and recorded at the other nodes within the network, reflecting the afferent and efferent pathways activated by DBS. Hippocampal activity, measured in LFP recordings, was altered by stimulation of the three targets differently, with parameter dependent effects that produced both excitatory and inhibitory changes in network state.

Conclusions

These results provide further insight into DBS effects within the Papez circuit, with possible implications regarding therapeutic mechanisms of action. The findings suggest potential stimulation strategies which may deserve further clinical evaluation, and reinforce the opportunities afforded by this new technology to study the effects of neuromodulation on brain function in completely new ways.

125: Monday, June 2, 2014, 4:35-4:45 pm; PS #3

Chronic Unlimited Recording Electrocorticography (CURE) Guided Resective Epilepsy Surgery: Beyond Subacute Monitoring - Technology-Enabled Enhanced Fidelity in Seizure Focus Localization with Improved Surgical Efficacy.

Daniel J. DiLorenzo, Erwin Zeta Mangubat, Marvin A. Rossi, Richard W. Byrne
Chicago, IL

Introduction

Epilepsy surgery is at the cusp of a technological transformation; of particular importance are chronic monitoring and neuromodulatory technologies. Chronic implanted neurological monitoring technology offers the potential to monitor patients chronically in their normal ambulatory setting with outpatient medication regimens. This overcomes significant temporal limitations, pharmacological perturbations, and infection risks inherent in present technology comprising subacute percutaneous inpatient monitoring of presurgical candidates.

Methods

In the pivotal study for the NeuroPace® Responsive Neurostimulation (RNS®) system, we assessed efficacy of the RNS® System to control seizures in patients with medically refractory epilepsy who were not candidates for further resective surgery. Beyond the scope of the pivotal study, we monitored seizure and epileptiform activity and performed long-term analysis of Chronic Unlimited recording Electrocorticography (CURE) from chronically implanted electrodes.

Results

Through long-term analysis of CURE from chronically implanted electrodes, we were able to further refine seizure source localization and sufficiently increase the expected likelihood of seizure control that four patients who had previously been considered not candidates for surgery did undergo resective surgery, and all have achieved seizure freedom.

Conclusions

CURE-guided resective epilepsy surgery employs new monitoring technology in a novel way, which in this small series was felt to improve seizure localization and consequently the potential efficacy of resective surgery. This suggests that the CURE modality could improve outcomes in patients who undergo resective surgery, and it may expand the set of patients in whom resective surgery may be expected to be efficacious and therefore the potential number of patients who may achieve seizure freedom. We report four patients in whom this technique and technology had a direct role in guiding surgery which provided seizure freedom, and we respectfully submit that this new approach warrants further study to characterize its value in pre-surgical evaluation.

126: Monday, June 2, 2014, 4:45-4:55 pm; PS #3
Relationship between Seizure Outcomes and MTLE Ablation Volumetrics for Stereotactic Laser Ablation

Anil Shetty, Chengyuan Wu, Brad Fernald, Ashesh Mehta, Michael Sperling, Ashwini Dayal Sharan
Philadelphia, PA, and Great Neck, NY

Introduction
Traditional surgical treatment provided seizure-free outcome in ~ 58 % of patients in the only randomized surgical trial for medically refractory temporal lobe epilepsy (TLE) patients, but is vastly underutilized. An exciting alternative is stereotactic laser ablation (SLA) that is minimally invasive. But, it is crucial to understand the ablation volume of the hippocampus and amygdala that needs to achieved to achieve seizure freedom.
Methods
13 medically-refractory patients (6mo - 2yr follow-up) with symptomatic localization-related TLE, underwent stereotactic frame-based placement of MR-compatible laser catheter (1.6mm diameter) through a 3.2mm twist drill hole. An FDA-cleared laser surgery system (Visualase; Visualase, Inc., Houston, TX) was utilized to monitor the ablation of epileptogenic foci with real-time MRI thermometry. Anatomical structures were manually segmented on pre-procedure volumetric data sets. Post-ablation volumes were generated by manually segmenting the ring enhanced ablation zone on a post-procedure T1 images. The two data sets were co-registered and percentage of amount of each structure ablated was calculated.
Results
11/13 patients had seizure reduction. 7(54%) out of the 13 patients achieved seizure freedom, 4(31%) had 75% or more seizure reduction and 2 patients had no change. The average percentage of ablated hippocampus and amygdala was about 60% and 45%, respectively. The percentage of amygdala ablated in seizure free group and non-seizure free group was 58% and 30%, respectively. 5/7 pts in seizure free group had smaller hippocampal volumes on ablated side. Two patients in non-seizure free group had bilateral foci and approach in another patient was inferior.
Conclusions
Seizure outcomes with SLA are comparable to the conventional surgical techniques. This volumetric analysis indicates relationship of success to atrophic hippocampi, >50% ablation of the amygdala and unilateral foci. More cases need to be analyzed to be indicative for seizure outcomes.

142: Tuesday, June 3, 2014, 11:54 am-12:00 pm; PS #5
Towards an Intelligent Neuroprosthetic System for Seizure Control: Hippocampal Dynamics in a Rodent Model of Focal Epilepsy

Babak Mahmoudi, Robert E. Gross
Atlanta, GA

Introduction
While selection of neurostimulation parameters for movement disorders such as tremor or Parkinson's disease involves choosing a setting and evaluating the immediate symptomatic response, the paroxysmal nature of epileptic seizures precludes this approach in neuromodulation therapies for epilepsy. We are developing a learning neuroprosthetic system for automatic parameter optimization using a metric during the interictal period. To this end we studied the interaction between the CA1 and CA3 in a rat tetanus toxin model of focal epilepsy.
Methods
Simultaneous Local Field Potential (LFP) signals in CA1 and CA3 were recorded chronically using microelectrode arrays in epileptic (tetanus toxin model) and control rats using a custom designed 16-electrode array with 8 microwire electrodes in CA1 and 8 in CA3. The functional interaction between CA1 and CA3 was compared between epileptic and control rats both at micro- and macro-temporal scales using wavelet coherence and correlation analysis in the principal component space, respectively.
Results
The macro-scale analysis demonstrated that in epileptic rats, the functional connectivity between CA1 and CA3 was significantly higher in epileptic rats compared to control rats. However, the dynamic range of the functional connectivity was significantly lower. A micro-temporal analysis during a pre-ictal phase in epileptic rats demonstrated abrupt rotations in the LFP phase between the CA1 and CA3. These rotations were frequency band-specific and were most prominent in the lower 10 Hz frequency band.
Conclusions
The results of our macro-temporal analysis suggest that CA1 and CA3 might be in a locked-in state in the tetanus toxin model. Also, using micro-temporal analysis we may be able to extract precise spatiotemporal signatures that predict the probability of seizure occurrence. The results of these findings can be used to define metrics that guide a learning neuroprosthetic system to optimize the neuromodulation parameters for eliminating or minimizing seizures and that discriminates between pathological and physiological patterns.

207 – Poster presentation

An Assessment of the Influence of Lesion Volume, Perilesional Resection Volume and Completeness of Resection on Seizure Outcome Following Surgery for Resection of Cortical Dysplasia in Children

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Washington, DC

Introduction
Focal cortical dysplasia (FCD) is one of the most common causes of intractable epilepsy leading to surgery in children. The predictors of seizure freedom following surgical management for FCD are still unclear. The objective of this study is a volumetric analysis of factors in the pre and post resection brain MRI scans of patients who had undergone resective epilepsy surgery for cortical dysplasia and the influence of these factors on seizure outcome
Methods
The medical records and brain imaging scans of forty three consecutive patients who had undergone surgical treatment for refractory epilepsy with focal MRI abnormalities and pathological diagnosis of FCD were reviewed. Preoperative lesion volume and postoperative resection volume were calculated by manual segmentation using Osirix-Pro software.
Results
Forty three patients underwent first time surgery for resection of cortical dysplasia. The age range at the time of surgery was 2 months to 21.8 years with a mean age of 7.3 years. Median duration of follow-up was 20 months. Mean age of onset was 31.6 months and a range of 1 day to 168 months. Complete resection of the area of focal cortical dysplasia as adjudged from the postoperative brain MRI scan was significantly associated with seizure control ($p = 0.0005$). Seizure control was not significantly associated with lesion volume ($p = 0.46$) or peri-lesional resection volume ($p = 0.86$)
Conclusions
Completeness of resection of radiological abnormality is a significant predictor of seizure freedom following resection of FCD in children. Lesion volume or further resection of perilesional tissue are not predictive of seizure freedom.

208 – Poster presentation

Precision of Robotic Depth Electrode Placement for Stereotactic EEG

Nitin Tandon
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Introduction
Stereo-electroencephalography (SEEG) is a minimally invasive, robust and precise method of localizing focal medically intractable epilepsy. Recently, a robot specifically designed for stereotaxis, has been available for SEEG electrode placement in the USA. The accuracy of this system in the clinical environment has never previously been validated.
Methods
The SEEG implantation plan was arrived at after a comprehensive review of the non-imaging data and after an in-depth discussion of the hypothesized region/s of seizure onset. Pre-operatively, T1 weighted MRI scans with contrast with 1x1x1 resolution were obtained. Planning of entry and target points was performed using robotic stereotactic software (ROSANNA). 5 skull fiducials were placed in each patient and a volumetric contrasted CT scan was obtained and co-registered with the MRI scan. The ROSA robot was registered to the skull fiducials and SEEG electrodes (PMT) were implanted. A volumetric CT scan was obtained post implantation and also registered to the planning MRI scan to measure deviations from the plan. The lateral deviation of each electrode at the entry point and at the target point was measured and compiled. The surgical time of electrode placement was also computed.
Results
Over 9-months, 200 SEEG electrodes were placed in 16 patients. There were no complications associated with electrode placement. Close review of the post-op imaging did not show any hemorrhages. The mean lateral error at the entry point was 0.64 mm (stdev 0.54) and at the target it was 1.10 mm (stdev 0.97). In all but 15 electrodes (7.5%), the error at the target was less than 2.5 mm. Average time for implanting each electrode was just under 9 minutes.
Conclusions
Robotic SEEG is a precise and rapid strategy for implanting electrodes for intracranial monitoring to pinpoint seizure foci. The use of skull fiducials may enable more precise placement than other registration techniques.

209 – Poster presentation

Increased Central Type Benzodiazepine Receptor Bindings Associated with Seizure Outcomes in Epileptogenic Frontal Cortical Dysplasia

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Okayama, Japan

Introduction
Single-photon emission computerized tomography (SPECT) analysis of central type benzodiazepine receptors binding by ^{123}I-labelled Iomazenil (IMZ) has been applied in some neuropsychiatric disorders. The deficit in central type benzodiazepine receptors indicated that abnormal synchronization was mediated by the lack of inhibitory postsynaptic mechanism. In this study we investigated IMZ SPECT in a small series of patients who harbored frontal focal cortical dysplasia presenting with seizures and were surgically treated in our institute.
Methods
Subjects were 17 patients with frontal lobe epilepsy due to focal cortical dysplasia, which was pathologically confirmed after resective epilepsy surgery. The preoperative interictal IMZ SPECT findings in these patients were reviewed retrospectively. The data were statistically analyzed using three-dimensional stereotactic surface projection (3D-SSP).
Results
Thirteen patients (80%) were seizure-free (Engel Class I). Decrease of IMZ uptake in the lesion (which means epileptogenic area) was observed in 13 patients. In addition, increase of IMZ uptake in the surrounding area of the lesion was recognized in 7 seizure-free patients. Both reduction of IMZ uptake in the lesion and increase of IMZ uptake in the surrounding area of the lesion were observed in 6 postoperative seizure-free patients and in only one patient with residual seizures after surgery. Intrestingly, increase of IMZ uptake in the contralateral side to the lesion was observed in 13 out of 17 patients. However there was no correlation between this result and seizure outcomes.
Conclusions
The increase in benzodiazepine receptor density surrounding the lesion is correlated with good surgical outcome. This might be related to the intrinsic antiepileptic mechanisms. Further studies are needed to clarify the mechanisms.

210 – Poster presentation

Anterior Temporal Lobectomy Compared with Laser Thermal Hippocampectomy for Mesial Temporal Epilepsy: A Threshold Analysis Study

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Introduction
Anterior Temporal Lobectomy (ATL) is the gold standard surgical treatment for refractory temporal lobe epilepsy; but it carries the risks associated with invasiveness, including cognitive decline and damage to eloquent structures. Laser thermal hippocampectomy (LTH) offers a less invasive alternative to the standard open approach. In this decision analysis, we determine the success rate at which LTH would be equivalent to ATL.
Methods
MEDLINE searches were performed for studies of anterior temporal lobectomy. Using complication and success rates from the literature, we constructed a decision analysis model for treatment with ATL and LTH. Utility values for the various outcomes and complications after ATL or LTH were extracted from literature examining patient preferences in similar clinical conditions. A sensitivity analysis in which major parameters were systematically varied within their 95% CIs was used.
Results
355 studies involving 26,251 cases of ATL were included. Outcomes of LTH are taken from a recently presented multicenter series of 68 cases. Sensitivity analysis revealed that probabilities of seizure control and late morbidity of LTH are most likely to affect outcomes compared to ATL. We calculated that LTH would need to stop disabling seizures (Engel class I) in at least 43% of cases and have fewer than 40% late mortality/morbidity to result in quality of life at least as good as that after ATL.
Conclusions
This decision analysis utilizing preliminary multicenter data suggests that LTH has similar utility to ATL. These early data support LTH as promising and less invasive alternative to ATL in refractory temporal lobe epilepsy. LTH utility may remain comparable to ATL even if long-term seizure control is less than that of ATL. Larger clinical studies will be needed to validate the true role of LTH in the refractory epilepsy patient population.

211 – Poster presentation

Chronic Sub-threshold Subdural Cortical Stimulation for the Treatment of Focal Epilepsy Originating from Eloquent Cortex

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Introduction
Despite advances in therapy, around 30% of patients with epilepsy remain medically refractory representing a major medical problem worldwide. While resection of a seizure focus may be curative, this option may be precluded if the focus resides in an eloquent region of cortex. This retrospective study reports our experience with a novel neurostimulation technique for the treatment of medically intractable focal seizures eminating from eloquent cortex.
Methods
We retrospectively identified three patients who underwent standard-of-care phase II EEG monitoring to localize the epileptic focus, which in each case was found to involve eloquent cortex. Trial focal cortical stimulation was then delivered through the monitoring grid utilizing the Medtronic model 37022 external neurostimulator and electrode configurations targeting the seizure focus, stimulation intensities (amplitudes and pulse durations) under the threshold required for motor or sensory activation, and both low (1 Hz) and high (100 Hz) frequencies. In two patients, a 4 x 4 stimulating grid created by juxtaposition of four Medtronic model 3587A Resume II electrodes was implanted and connected to a Medtronic model 37712 Restore Ultra allowing for chronic stimulation.
Results
All three patients had a significant reduction in seizures during the trial period of stimulation including immediate arrest of epilepsia partialis continua (EPC) in two. One patient declined permant implanation. Of the two permanently implanted, one remained seizure free at two years, and the other experienced reduction in seizure counts from 15 daily to 1-4 monthly at 16 months. No additional morbidity was associated with the trial stimulation or permanent implantation.
Conclusions
This small case series provides some evidence for efficacy of targeted continuous neocortical stimulation in the treatment of medically refractory focal epilepsy and may support ongoing investigations into this treatment modality.

212 – Poster presentation

A Decision Tree Analysis of Volumetrics in Temporal Lobe Epilepsy

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Detroit, MI

Introduction
Changes in brain volume of various structures have been implicated in temporal lobe epilepsy (TLE). Although decreased volume of a hippocampus has long been associated with laterality in TLE, we sought to determine if there was a better marker that might obviate the need for Phase II monitoring.
Methods
Using Freesurfer, we extracted the volumetric attributes on forty-one different structures from preoperative images of seventy-five retrospective TLE patients with surgical outcome of Engel class I. Using a correlation-based subset evaluator of attribute, we selected a subset of prominent structures with high predictive ability of lateralization class and measured the lateralization accuracy rate by each individual structure. As the selected features may covary, we obtained an optimum combination set by computing information gain with the J48 decision tree algorithm.
Results
In feature selection phase, some structures, e.g., Hippocampus, Cerebral-White-Matter, Thalamus-Proper, Thalamus and Choroid-plexus performed better than other structures. Among these structures, Hippocampus is the best individual predictor of Engel I outcome. A J48 decision tree with use of volumetric features of individual hippocampus structures achieves 80% lateralization accuracy rate. The best combination subset of features is observed for combining the volumetrics of the hippocampus and amygdala, for which 86.7% lateralization accuracy rate is achieved. Rules extracted from the tree demonstrate that asymmetry in amygdala volume can be used to determine laterality in patients with negligible asymmetry in hippocampal volume.
Conclusions
This study confirms the importance of hippocampal volume in determining laterality in TLE. Decision tree analysis demonstrates that a combination of hippocampal and amygdalar volumetrics has superior predictive value to other individual or combined structures.

213 – Poster presentation

Surgery of Pure Insular Non Tumoral Epileptic Foci Explored by SEEG

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Introduction
Hidden by the perisylvian operculi, insular cortex has long been under-explored in the field of epilepsy surgery. Recent studies advocate stereo-electroencephalography (SEEG) as a reliable tool to explore insular cortex and its involvement in intractable epilepsy, and suggest that insular seizures could be an under-estimated entity. However insular resection is scarcely reported as a therapeutic option. The authors report here 6 cases of right insular resection based on anatomo-electroclinical correlations provided by SEEG.
Methods
6 right handed patients (3 males, 3 females) with drug-resistant epilepsy, underwent comprehensive presurgical evaluation. Based on video-EEG recordings, they all underwent SEEG evaluation with bilateral (n=4), or unilateral right (n=2) insular depth electrodes placement. All patients had both orthogonal (4 to 6) and parasagittal (1 anterior, 1 posterior) transinsular electrodes. Preoperative MRI was normal in 4 cases, 1 patient had right insular focal cortical dysplasia, 1 patient had a right opercular postoperative scar (cavernous angioma). All patients underwent right insular corticectomy by subpial, transopercular approach.
Results
Intracerebral recordings confirmed “pure” right insular epileptogenic zone in all patients. After surgery, 5 of 6 patients were seizure-free (Engel I) with a mean follow up of 29.2 months (10-66), and the latter had a significant reduction in seizure frequency (Engel IIIa). Histological findings revealed a focal cortical dysplasia in 5 cases , and one case of gliosis scar. All patients had minor transient neurological deficit (facial paresis, dysarthria).
Conclusions
Orthogonal plus parasagittal transinsular electrodes provide a large scale exploration, and lead to identify epileptic foci confined within the insula with high reliability. Insular corticectomy cured 5 out of 6 patients without permanent neurological deficit. These results suggest that SEEG should be performed more systematically when insular epilepsy is suspected even if preoperative MRI is normal, and corticectomy should legitimately considered as a safe option for curative purposes.

214 – Poster presentation

Seizure and Cognitive Outcomes after Stereotactic Laser Amygdalohippocampotomy for Mesial Temporal Lobe Epilepsy: Series of 27 Patients

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Introduction
Stereotactic laser amygdalohippocampotomy (SLAH) - ablation of the mesial temporal region using laser interstitial thermal therapy (LITT) - is a new, minimally-invasive alternative to open mesial temporal resections that may offer lower surgical morbidity with similar effectiveness in well-selected cases.
Methods
In a prospective observational study, twenty-seven patients underwent SLAH (18L, 9R) between July, 2011 and February, 2014. Nineteen had mesial temporal sclerosis (MTS) on MRI, 5 had normal MRI, and 3 had T2 signal change or atrophy only. All were candidates for open mesial temporal resection, and both procedures were offered.
Results
Of 14 patients who have reached 6 months follow-up, 8 have been seizure-free (57%); 4 have been seizure-free for 15 – 26 months, and no patient who was seizure-free at 6 months has recurred. Seven of 10 patients (70%) with MTS, and 8 of the last 11 patients (73%) are seizure-free, likely reflecting a learning curve. Of the 6 patients who are not seizure-free: 2 have >85% seizure-reduction (1 of whose recurrent seizures are contralateral, and one of whom has bilateral MTS); 2 underwent ipsilateral mesial temporal resections (1 of whom became seizure-free); and 1 underwent a second ablation after 6 months. Persistent complications included one permanent homonymous hemianopia (3.7%), early in the series. Length of hospital stay was 1.7±0.8 days (mean±S.D.; median = 1; range 1-3). The first 10 patients reaching 6 month follow-up testing showed no significant decline on naming, object recognition, verbal fluency, or episodic memory.
Conclusions
In this initial cohort, the seizure-free rate after SLAH was comparable to open resection, especially when considering patients with MTS, with notably superior post-operative cognitive testing. For a substantial proportion of patients who are candidates for mesial temporal resection, SLAH may offer seizure-freedom after a 1-day hospital stay, with minimal perioperative discomfort, and improved neurocognitive performance post-operatively.

215 – Poster presentation

Methodology for Critical Evaluation of Appropriate Targets in Stereotactic Laser Ablation for Mesial Temporal Lobe Epilepsy: A Pilot Study

Chengyuan Wu, Richard Gorniak, Meela Mehdi, Michael Sperling, Christopher Skidmore, Ashwini Dayal Sharan
Philadelphia, PA

Introduction

Stereotactic laser ablation (SLA) is a promising minimally-invasive alternative for treating of mesial temporal lobe epilepsy (MTLE). While our experience to date has suggested that seizure outcome may not be directly associated with total ablation volume, the specifics of the relevant variables remain unclear. We therefore formulated and tested a methodology to critically evaluate the suitability of specific targets in SLA for MTLE.

Methods

We performed a single-center retrospective cohort study involving 10 consecutive patients undergoing SLA for MTLE at Thomas Jefferson University. Preoperative non-contrast MRIs served as reference images, which were segmented with FreeSurfer. Postoperative gadolinium-enhanced MRIs were coregistered to the preoperative image using SPM8. Ablation volumes including the gadolinium-enhancing component were manually segmented from coregistered images. These volumes were superimposed upon the initial segmentation to determine the percentage of each structure ablated. Since the sample size inadequately powered formal statistical analysis, mean ablation volumes between 'seizure-free' (SF) and 'not seizure-free' (NSF) subgroups were compared.

Results

Mean hippocampal volumes were lower on the side of reported HS, while volumes of other mesial structures were comparable. Eight patients with at least 3 months follow-up were included in volumetric analysis. Hippocampus and amygdala ablation volumes were larger for the SF subgroup, while the affected volumes of all other mesial structures were smaller.

Conclusions

The presented methodology allowed for critical evaluation of relative volumes of mesial structures affected by SLA. Preliminary results suggest the importance of ablation accuracy – greater hippocampal and amygdala coverage with targeting of the anterior and lateral aspects may be associated with better seizure outcomes. Anatomically, targeting the lateral hippocampus may focus more on the CA1 region, which has been implicated in epileptogenesis in MTLE. Further studies with supervised segmentations and long-term follow-up are necessary to substantiate these preliminary findings.

216 – Poster presentation

Electrical Stimulation of the Anterior and Centromedian Nucleus of the Thalamus for Treatment of Refractory Epilepsy — Report of Four Cases

Wei Hu, Jian-Guo Zhang, Bryan T. Klassen, Fan-Gang Meng, Daniel A. Clayton, Kendall H. Lee, Matt Stead
Rochester, MN, and Seattle, WA

Introduction

Although many of medically intractable patients have good responses to established surgical management, a substantial proportion of patients are still refractory to these therapies. Over the last decade, experimental and clinical studies have suggested that electrical deep brain stimulation (DBS) of subcortical structures is a promising therapy for patients with refractory epilepsy. Both the centromedian (CM) and anterior nuclei (AN) of the thalamus have been targets for DBS to control epilepsy, with a suggestion that each may be preferentially effective for different seizure types. Patients with multiple seizure types might benefit from implantation of electrodes at both target sites.

Methods

Four intractable epilepsy patients with DBS implantation were retrospectively assessed. These patients were either not candidates for resective surgery or refractory to the treatment of vagus nerve stimulation and/or resection surgery. All patients underwent bilateral thalamic AN and CM DBS simultaneously. Two patients were admitted to the epilepsy monitoring unit (EMU) for further DBS programming based on their EEG recording results.

Results

One male and three female patients with median age of 14 years (range 5-19 years) at surgery underwent DBS. Median duration of epileptic history was 11 years (range 4-18 years). All patients recuperated well from the surgical procedure and post-operative MRI documented that all electrodes were correctly located. Average postoperative follow-up was 16 months (range 13-18 months). The average seizure frequency reduction was 63 percent. One patient had been seizure free for 12 months. Additionally, one patient experienced wound dehiscence requiring revision of the generator; otherwise no complications occurred.

Conclusions

These findings suggest that simultaneous bilateral stimulation of the AN and CM of the thalamus could potentially reduce seizures in medically refractory epilepsy patients who were either refractory to VNS, or not candidates for resective surgery. DBS programming based on EEG recording results is useful for seizure management.

217 – Poster presentation

Extraoperative Cortical Stimulation in Localization and Mapping of Eloquent Areas during Epilepsy Surgery

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Larissa, Greece

Introduction
Surgical resection of epileptogenic focus/i constitutes a standard surgical strategy in the management of patients with well-localized, medically refractory epilepsy. However, despite the recent advances in functional MR imaging, identification and exact localization of eloquent cortical areas still remains quite puzzling, especially in cases of language associated cortical areas. Intraoperative direct cortical stimulation has occasionally been associated with patient's discomfort and failure of completing the mapping procedure. Extraoperative cortical stimulation through previously implanted subdural electrodes may provide an alternative option in identifying and mapping eloquent cortical areas. In our current study we present our experience with employing this methodology in patients undergoing surgery for medically refractory epilepsy.
Methods
A total of 46 patients (28 M and 18 F) suffering medically intractable epilepsy were implanted with subdural grid and strip electrodes. All patients underwent extraoperative electrical cortical stimulation for motor, sensory, and language cortical areas localization. Cortical resections were planned according to the stimulation findings, and were performed through a second procedure. The participants were evaluated postoperatively (immediately and after 4 weeks) for any procedure-related neurological deficits.
Results
Extraoperative mapping was possible in all cases. Mapping was completed in three sessions in 1 patient (2.2%), in two sessions in 7 pts (15.2%), and in a single session in 38 pts (82.6%). The duration of mapping procedure ranged between 134 to 450 min (mean: 227.9). A new neurological deficit was evident immediately postoperatively in 6 pts (13.0%), while remained in only 2 pts (4.4%) at 4 weeks after surgery. Seizures during the stimulation process occurred in 15 pts (32.6%).
Conclusions
Extraoperative cortical stimulation represents a valid option for mapping, in patients undergoing epilepsy surgery. It accurately localizes eloquent cortical areas with high reliability and reproducibility, while it ensures the patient's comfort and cooperation.

218 – Poster presentation

Outside the Box: A Method for Targeting Stereo-electroencephalography (sEEG) Electrodes with the CRW Stereotactic Frame in "Mohawk" (Sagittal) Orientation in the Absence of Appropriate Supporting Software

Jon Timothy Willie, David Lozada, Robert E. Gross
Atlanta, GA

Introduction
Vascular neuroimaging and rigid frame stereotaxis (e.g. CRW, Leksell) are critical for precise placement of multiple sEEG depth electrodes. Lateral (e.g. transtemporal) trajectories are attained with frames in sagittal, or "Mohawk" orientation. However, Framelink® software on the Stealth® workstation (Medtronic) does not accommodate Mohawk orientation, failing to provide appropriate trajectory angles. Pending a software update, and in lieu of purchasing alternative software that supports this orientation (e.g. BrainLab), we describe our experience with a simple workaround utilizing the CRW phantom and a 2nd CRW frame to generate the ring and arc angles.
Methods
For frames in sagittal orientation, FrameLink software generates inappropriate angles or error messages in the frame coordinates screen. However, Framelink displays lateral (lat), anterior/posterior (A/P) and vertical (vert) stereotactic frame coordinates at any desired point along a planned trajectory. To determine trajectory angles, we set the CRW frame for the lat, A/P and vert coordinates of the target, and attached this to the phantom, which was set to lat, A/P and vert coordinates of another point anywhere along the trajectory. The ring and arc angles are then adjusted such that the target-centered arc pointer precisely intersects the tip of the phantom target. The resulting angles yield the sole geometric solution for the planned trajectory. We prefer to determine angles off the sterile field using a 2nd frame, allowing the sterile frame to remain on the base-ring at all times and to be adjusted using the angles read off the non-sterile frame.
Results
By this method, we placed 144 depth electrode in 15 patients over 13-months. Accuracy with this method was superior to frameless image-guided stereotaxis. No hemorrhagic complications were encountered.
Conclusions
The arc-based geometry of target-centered frames enables a simple workaround for lateral stereotactic trajectories using the CRW frame and phantom without software supporting the Mohawk orientation.

219 – Poster presentation

Vagus Nerve Stimulation – Finite Element Model of the Nerve and Electrode

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Boston, MA, and Burlington, MA

Introduction

Vagus Nerve Stimulation (VNS) has been available clinically since the FDA approved it in 1997 but its mechanisms of action against epilepsy or other disorders (eg. depression) remain unclear. The basic theory is that stimulating the vagus nerve leads to activity in first the nucleus of the solitary tract (NST) in the brainstem, primarily, followed by activation or inhibition of multiple other brain centers which may be important in seizure propagation, somehow inhibiting seizure progression. We have started to investigate such a theory by using a computational model of the vagus nerve and the electric field within it as a first step to understanding what activity reaches the NST with typical stimulation.

Methods

Similar to the approach by Helmers et al., we have created a finite element model (FEM) of the vagus nerve divided into typical multiple fascicles and taking into account tissue impedance and other parameters as well as the precise electrode design and configuration. We have run this in COMSOL software and use a previously published method to calculate the likely number and location of activated axons within the nerve using typical stimulation levels.

Results

Graphical representation of the electric field and gradients within the vagus nerve during stimulation are produced and relative numbers of fiber diameters that likely reach threshold are calculated.

Conclusions

This is a first step toward integrating electric field output of FEM and a detailed computational model of the NST circuitry. Tying together clinically relevant stimulation parameters with effects on the circuitry will address potential mechanisms of action in VNS. Such studies may lead to the development of more effective stimulation patterns, energy usage, and programming efficiency.

123: Monday, June 2, 2014, 4:15-4:25 pm; PS #3
Anterior Thalamic Deep Brain Stimulation: BOLD Activation Patterns in a Large Animal Model

William Gibson, Seong Rok Han, Erika K. Ross, Ju Ho Jeong, Joo Pyung Kim, Jamie Joseph Van Gompel, Kevin Bennet, Kendall H. Lee, Paul Hoon-Ki Min
Rochester, MN

Introduction
The Electrical Stimulation of the Anterior Thalamus for Epilepsy (SANTE) trial has provided randomized data that deep brain stimulation (DBS) of the anterior thalamic nucleus (ATN) has clinical efficacy for the treatment of medically refractory complex partial seizures. While the mechanism of action underlying ATN DBS remains poorly understood, the therapy clearly exerts its effect distantly from the seizure onset zone by modulation of neural networks. Here we investigate the activation patterns induced by ATN DBS in a large animal model by monitoring the blood oxygenation level-dependent (BOLD) response on fMRI.
Methods
We performed DBS in anesthetized swine, targeting the left ATN (n = 3), and applied stimulation parameters which replicate the median values used in the SANTE trial (145 Hz, 5V, 90 us; 1 minute on, 5 minutes off) as well as brief stimulation (6 seconds on, 1 minute off) and measured the resulting BOLD activation patterns with 3T fMRI.
Results
We found that ATN DBS resulted in widespread ipsilateral activation of cortical areas, most robustly in the temporal lobe, but also in the premotor cortex, primary motor and somatosensory cortices, cingulate cortex, and insula. Varying DBS voltage and frequency, we found that the cluster size of BOLD activation increased. Notably, with stimulation at 8 V and 60 Hz, we observed bilateral temporal and frontal activation patterns.
Conclusions
These results show that ATN DBS is capable of inducing activation in a wide variety of cortical structures, and that the size of activation areas is strongly amplitude- and stimulation time-dependent. Therefore, this treatment may hold untapped promise for the treatment of seizures with both intra- and extratemporal foci, and the mapping of the DBS circuitry effect in relation to these foci with fMRI may prove clinically useful in the future.

140: Tuesday, June 3, 2014, 11:42-11:48 am; PS #5
MRI-guided Stereotactic Laser Ablation of Presumed Cavernous Malformations in Drug-resistant Epilepsy

D. Jay McCracken, Robert E. Gross, Jon Timothy Willie, David Lozada
Atlanta, GA

Introduction
Open surgical resection is generally indicated for symptomatic cavernous malformations, including those associated with medically refractory epilepsy. Minimally invasive alternatives may maintain therapeutic efficacy while minimizing complications and disfigurement. MRI-guided stereotactic laser ablation (SLA) is a novel, FDA-cleared, minimally invasive approach to treating lesional epilepsy and brain tumors, including deep-seated lesions. To date, this approach has not been reported for cavernous malformations (CM). We present a case series of SLA of presumed CM causing refractory epilepsy.
Methods
Five patients with medically refractory epilepsy undergoing standard presurgical evaluation (3-Tesla MRI, fluoro-deoxyglucose PET, neuropsychological evaluation, and inpatient video-EEG studies) were found to have corresponding lesions consistent with CM. Each underwent stereotactic placement of a laser fiber assembly (optical fiber in a saline-cooled 1.6-mm diameter catheter, Visualase, Inc.) via twist drill hole under general anesthesia. Real-time MR anatomic and thermal imaging verified placement and extent of ablation of CM and surrounding cortical rim during ablation with a 15W diode laser.
Results
MR imaging revealed no evidence of hemorrhage following fiber placement within presumed CM. Immediate post-procedure contrasted imaging confirmed ablation in all cases. We detected no adverse events or neurological deficits. No ICU admissions were indicated and patients were discharged the following day. Three patients with temporal lobe lesions are seizure free at 6-15 months follow-up. One patient with a frontal lobe lesion has had a significant reduction in seizure frequency and severity, but is not seizure-free. It is too soon for seizure follow-up on the most recent patient.
Conclusions
Minimally invasive MRI-guided SLA of presumed epileptogenic CM is a potentially safe and effective alternative to open resection. We have performed this procedure without complication in five patients who have experienced excellent seizure outcomes. With additional experience this technique may become an excellent first option for patients with this disorder.

141: Tuesday, June 3, 2014, 11:48-11:54 am; PS #5
Postoperative Plasticity after Cingulotomy in Patients with Obsessive-Compulsive Disorder

Garrett P. Banks, Charles Mikell, Emad N. Eskandar, Sameer A. Sheth
New York, NY, and Boston, MA

Introduction
Stereotactic cingulotomy has been used to treat severe, refractory obsessive-compulsive disorder (OCD) for decades. However, while cingulotomy is believed to disrupt reentrant fronto-striato-thalamic circuitry (FSTC), how cingulotomy modifies this circuit is unknown. We retrospectively analyzed preoperative and postoperative neuroimaging, using diffusion tensor imaging (DTI) and voxel based morphometry (VBM) techniques, in patients who underwent cingulotomy for OCD, to determine how non-lesioned sites adapted postoperatively.
Methods
Five patients were selected who received preoperative and one year postoperative volumetric T1 images. For each patient, whole brain gray matter partial volume changes were calculated in MNI standard space using the FSL VBM toolkit. Results were cluster thresholded for significance using the FSL program easythresh. Additionally, four patients were selected who received diffusion tensor imaging both one year postoperatively, and either immediately before or after the surgery. FSL's tract based spatial statistics (TBSS) toolkit was used to construct patient specific fractional anisotropy skeletons, and the mean fractional anisotropy (FA) of the left and right anterior internal capsule was analyzed over time on a patient-specific basis.
Results
A significant gray matter volume reduction occurring over the postoperative year was seen for all patients in a right-sided cluster spanning the dorsolateral prefrontal, superior frontal and paracingulate cortex ($p = 0.008$, corrected for multiple comparisons by threshold free cluster analysis.). Anterior internal capsule FA changes were then plotted for each of the four patients. Compared to preoperative FA, a postoperative decrease in FA was seen in all patients at all time points in the right anterior internal capsule. While there were some decreases in FA on the left, this was not consistent across subjects.
Conclusions
Cingulotomy results in secondary alterations of the right prefrontal cortex and right anterior internal capsule, which develop within one year of surgery. These findings suggest that post-operative plasticity may account for some of the therapeutic effects of cingulotomy. Increased understanding of these circuits will assist with the development of novel therapies for OCD.

143: Tuesday, June 3, 2014, 10:15-10:25 am; PS #6
Fornix High Frequency Stimulation Induces BOLD Change and DA Release in Hippocampal and Mesolimbic Circuitry

Erika K. Ross, Paul Hoon-Ki Min, Joo Pyung Kim, Seong Rok Han, Kendall H. Lee
Rochester, MN

Introduction
Deep brain stimulation (DBS) has recently been applied in the Papez circuit to improve memory function associated with dementia. As part of this circuit, the fornix plays an integral role in declarative memory, and is currently investigated as a potential DBS target. Here, we hypothesize that fornix DBS results in widespread activation of the Papez circuitry with underlying neurotransmitter release. To test this hypothesis, we characterized fornix stimulation-induced functional activation by fMRI and associated neurochemical release using fast scan cyclic voltammetry (FSCV) in a large animal model of DBS.
Methods
An in-house developed MR image-guided stereotactic targeting system was used for DBS electrode (Medtronic 3389) targeting and implantation in 7 domestic pigs (30±3 kg). fMRI experiment and data analysis was performed on a 3.0T GE scanner, using a block design of 6 seconds stimulation and 60 seconds rest. For FSCV studies, a carbon fiber microelectrode (CFM) was used to detect dopamine (DA) release with our wireless instantaneous neurotransmitter concentration system (WINCS).
Results
Fornix DBS resulted in significant BOLD changes within Papez circuitry regions, including hippocampus, entorhinal cortex, and parahippocampal gyrus (FDR < 0.001). Additionally, we observed BOLD changes in mesolimbic structures including nucleus accumbens, and prefrontal cortex. Lastly, we found stimulation time locked DA release in the nucleus accumbens using FSCV.
Conclusions
Taken together, the fMRI activation pattern combined with observed DA release in the nucleus accumbens, support the hypothesis that fornix DBS results in widespread activation of the Papez circuitry with underlying neurotransmitter release. Further, our results support the exciting possibility that the neuromodulatory effect seen here may play a role in the therapeutic effect seen with fornix DBS in improving memory.

144: Tuesday, June 3, 2014, 10:25-10:35 am; PS #6

Structural Changes in Brain Circuits of Patients with Alzheimer's Disease Undergoing Deep Brain Stimulation

Tejas Sankar, Mallar Chakravarty, Agustin Bescos, Monica Lara, Toshiki Obuchi, Adrian Walter Laxton, Mary Pat McAndrews, David Tang-Wai, Gwenn Smith, Clifford Workman, Andres M. Lozano
Edmonton, Alberta, Canada, Winston-Salem, NC, and Toronto, Ontario, Canada

Introduction
Deep Brain Stimulation (DBS) is thought to ameliorate symptoms in selected neurological disorders by modulating pathological activity within dysfunctional brain circuits. To date, there is no evidence that DBS counteracts neurodegeneration. We hypothesized that DBS applied to the fornix in patients with Alzheimer's Disease (AD) might be neuroprotective, impacting brain structure particularly in the human memory circuit.
Methods
In six patients with early AD receiving fornix DBS, we used structural MRI to assess one-year change in hippocampal, fornix, and mammillary body volume. We also used deformation-based morphometry to identify whole-brain structural changes. We correlated observed volumetric changes to hippocampal glucose metabolism. We also compared volumetric changes to those in an age-, sex-, and severity-matched group of AD patients (n=25) not receiving DBS.
Results
We found sizeable bilateral hippocampal volume increases (between 5-9%) in the two patients with the best clinical response to fornix DBS, which is unexpected in the setting of AD. In one of these patients, there was no progression of hippocampal atrophy fully three years after diagnosis. Overall, the mean rate of hippocampal atrophy was significantly slower in the DBS group compared to the matched AD group ($p<0.05$, paired t-test), and none of the matched AD patients demonstrated bilateral hippocampal volume increase. Across DBS patients, hippocampal volume change correlated strongly with hippocampal metabolism and with volume change in the fornix and mammillary bodies, suggesting a circuit-wide effect of stimulation. Finally, whole-brain analysis in DBS patients revealed local volume expansions in several regions which typically demonstrate progressive atrophy in AD.
Conclusions
We the present the first in-human evidence that, in addition to modulating circuit activity and providing symptomatic relief, DBS may influence the natural course of brain atrophy in neurodegenerative disease. This raises the possibility that, in selected disorders, DBS may slow disease progression in a clinically beneficial manner.

146: Tuesday, June 3, 2014, 10:45-10:55 am; PS #6

Brain Edema around DBS Leads and Ventricular Catheters: Clinical Characteristics, Radiological Similarities and Differences.

Kathryn L. Holloway, Viktoras Palys, Marie Bradley, Miriam L. Hirsch, Jackie Johnson
Richmond, VA

Introduction
The delayed onset of brain edema around DBS leads has been reported by several groups. To our knowledge, no studies up to date have identified the etiopathophysiology of such edema. It is unknown whether this phenomenon is unique to deep brain stimulators or if it is common to other cerebral implants as well.
Methods
We retrospectively reviewed the clinical and radiological data of our patients who presented with delayed onset of neurological decline within the first 2 weeks of DBS surgery. Comparison was made with a cohort of patients who underwent placement of ventricular catheters (ventriculostomies or ventriculoperitoneal shunts) during the same time period.
Results
In 2011-2013, 140 patients had DBS systems implanted. Seventeen patients demonstrated unexplained delayed neurological decline. Imaging studies revealed that 11 of these patients (7.9% incidence) had developed brain edema around the DBS leads. 12 patients (20% incidence) in the comparison cohort developed brain edema post-procedurally around the ventricular catheters. Radiologically, the temporal course and edema pattern of white matter involvement were strikingly similar to the DBS patient's scans with the edema extending down the length of the implant. In contrast to the DBS patients, two thirds of the ventricular cases had a small amount of blood at the cortical entry site. None of our DBS patients had acute blood visible on postoperative CT, however, a single patient's MRI revealed small bleeds that were easily obscured on CT by metal artifacts from DBS leads. Interestingly, the edema around ventricular catheters never achieved the impressive volumes of the peri-DBS edema. All DBS patients with brain edema demonstrated a benign clinical course. These and other features are discussed in more detail.
Conclusions
The brain tissue penetration during hardware insertion is the most conspicuous feature unifying radiologically quite similar incidence and distribution of brain edema around DBS leads and ventricular catheters.

150: Tuesday, June 3, 2014, 11:25-11:35 am; PS #6

Convection Enhanced Delivery Guided DBS Electrode Placement for Stereotactic Surgery to Improve Placement Accuracy

Aaron E. Bond, Robert Dallapiazza, George Gillies, W. Jeffrey Elias
Charlottesville, VA

Introduction
Stereotactic surgery depends upon precision. Traditionally, treatments are confirmed with awake intraoperative clinical and electrophysiologic verification; but image-guided surgery has more recently been proposed as CT and MRI systems become available in the operating room. We are developing a new technique which uses convection enhanced delivery (CED) to manipulate the extracellular space, thus enhancing the MR imaging of deep, subcortical structures. This technique could greatly improve the accuracy and success of stereotactic surgery, and could eliminate the reliance on awake surgery.
Methods
An FDA-approved, Evitar™ intracerebral catheter was stereotactically inserted into basal ganglia in twelve swine, so that various infusates could be convected with concurrent MRI at a flow rate of 5 microliters / hour. The infusions were monitored every 15 minutes with T2 weighted images. The swine were then clinically observed and sacrificed for histological analysis.
Results
Volumes as small as 15 microliters become apparent with T2 MRI. Further infusion highlights the distinction between white and gray matter – thus enhancing the visualization of deep brain nuclei and anatomy. As the volume of distribution increased, the basal ganglia nuclei and deep brain anatomy became well defined. Histological analysis demonstrated no damage to neurons when the correct infusate is chosen.
Conclusions
This work provides the initial foundation of a novel approach for higher precision visualization of the deep brain structures during stereotactic procedures. Convective infusion alters the extracellular water content of brain for improved MR imaging. Preclinical safety testing in a large brain, animal model is now complete, and a clinical trial is being designed to assess the feasibility in patients with movement disorders.

220 – Poster presentation

Optimization of 1.5 T fMRI Imaging during Deep Brain Stimulation detects activation in motor and non-motor circuitry

William Gibson, Paul Hoon-Ki Min, Emily Knight, Joel P. Felmlee, Krzysztof R. Gorny, Kirk M. Welker, Bryan T. Klassen, Su Youne Chang, Kendall H. Lee
Rochester, MN

Introduction
Intraoperative fMRI is potentially a powerful technique to visualize global circuitry modulation by Deep Brain Stimulation (DBS), but human studies have been plagued by concerns over the safety of fMRI in patients with implanted devices. We describe a safe and effective methodology to perform 1.5T intraoperative fMRI during DBS in the largest series of patients reported to date. Using this methodology, we test the hypothesis that DBS of movement disorder targets (subthalamic nucleus - STN, globus pallidus interna - GPi, and ventral intermediate thalamus - VIM) leads to differential areas of blood oxygen level dependent (BOLD) signal activation.
Methods
Eight patients (n=4 STN for Parkinson's disease, n=2 VIM for essential tremor, and n=2 GPi for dystonia) underwent intraoperative 1.5T fMRI during block design stimulation delivered via an external pulse generator. All pulse sequences used in the study were first extensively safety-tested in an anthropomorphic phantom.
Results
DBS of VIM and GPi resulted in activation of motor circuitry, with VIM DBS activating primary motor cortex and GPi DBS activating putamen, substantia nigra, and subthalamic nucleus. In contrast, DBS of STN for PD resulted in activation of both motor and non-motor circuitry, including premotor and supplementary motor cortices, thalamus, and limbic circuitry, including cingulate and insula.
Conclusions
1.5T fMRI can safely and reproducibly detect global circuitry modulation in patients during DBS. DBS of different targets for movement disorders resulted in distinct patterns of motor and non-motor circuitry activation which may underlie the therapeutic effects and side effects.

221 – Poster presentation

Use of an Acellular Dermal Matrix to Improve Cosmesis and Provide a Layer of Protection to DBS implants

Lisa Anne Feldman, Marie Bradley, Miriam L. Hirsch, Kathryn L. Holloway
Richmond, VA

Introduction
Deep brain stimulators (DBS) provide excellent control of tremor and dystonia in patients with movement disorders. As movement disorders often affect older patients, DBS are commonly placed in balding men. Typically, the scalp becomes thin and atrophic as the patient balds. This thin skin often becomes a shrink wrap over the implant, providing poor cosmesis and vulnerability to erosion and laceration. In order to overcome these issues, our group has evaluated two forms of acellular dermal matrix to augment soft tissue coverage in the scalp.
Methods
We implanted DBS and acellular dermal matrix in 50 of patients over a two year period. A small piece of acellular dermal matrix was cut to cover the burrhole cap and connector to the extensions. The overlaying dermis was approximated with Nylon. We followed the patients post-operatively for cosmetic outcome.
Results
Acellular dermal matrix derived from fetal bovine skin provided excellent coverage and was not associated with serous drainage. The wounds healed well, with improved cosmetic outcome. In two instances the implant provided a barrier to contamination of the hardware when the wound dehisced.
Conclusions
The inclusion of fetal bovine acellular dermal matrix in cutaneous closures adds an extra layer of protection over the leads to prevent erosion through the skin, and adds smoothness for improved cosmetic outcome.

222 – Poster presentation

A Wound Revision Strategy for Deep Brain Stimulation Surgical Site Infection

Ephraim W. Church, Gareth M. Davies, James McInerney
Hershey, PA

Introduction
Permanent hardware implantation is integral in functional neurosurgery, and wound dehiscence and infection can jeopardize the success of an operation. Despite progress in identifying factors that may reduce the incidence of surgical site infection (SSI), this problem cannot be completely eradicated. Traditionally, SSI in the presence of hardware is treated with hardware removal. We sought to determine whether a strategy of initial treatment with wound revision could prevent hardware removal in deep brain stimulation (DBS) surgery.
Methods
We reviewed all DBS surgeries performed by one surgeon at our medical center from 2004-2013. We examined each SSI treated with wound revision and whether hardware removal was required subsequently.
Results
We identified 344 bilateral or unilateral lead implantation surgeries, each of which involved two surgeries for lead implantation and pulse generator placement. Thirty-six washout procedures were performed. Twenty-two of these did not require hardware removal, yielding a strategy success rate of 61%.
Conclusions
An initial strategy of wound revision can prevent ultimate hardware removal in the majority of DBS SSI. In an era of increased hardware implantation and cost awareness, these data can help guide management of SSI.

223 – Poster presentation

Interstitial Brachytherapy with Iodine-125 Seeds for Low Grade Brain Stem Gliomas in Adults: Diagnostic and Therapeutic Intervention in a One-Step Procedure

William Omar Contreras Lopez, Michael Trippel, Soroush Doostkam, Thomas Reithmeier
São Paulo, Brazil, and Freiburg, Germany

Introduction

Brainstem glioma in adults is a rare and poorly characterized disease. Therapeutic alternatives are mainly limited to external beam radiation as surgery is only indicated for exophytic tectal gliomas and the role of chemotherapy is still undefined. However several reports in the literature underlined the necessity to confirm histopathologically the presence of a brain stem glioma due to diagnostic inaccuracy of preoperative magnetic resonance imaging (MRI). Therefore we suggest the management of patients with brain stem glioma by stereotactic biopsy and implantation of I^{125} seeds for interstitial radiosurgery in a single step procedure as an alternative to external radiation therapy.

Methods

Ten patients with well-circumscribed lesions of the brainstem and histological confirmation of low grade glioma treated with stereotactically implanted I^{125} seed in our department between 1995 and 2012 were retrospectively analyzed.

Results

In 9 patients the lesion was treated with one I^{125} seed and in one patient, 2 spatial separated lesions were implanted, therefore a total of 11 I^{125} seeds were implanted. The mean volume of the 11 lesions was 2.76 ml (range 0.5–7.2 ml), mean activity of the seeds was 6.23 mCi (range 1.5–11.1 mCi), mean duration of irradiation was 28.5 days (range: 21–41 days) and mean effective dose rate was 9.16 cGy/h (range 6.2–12 cGy/h). The 30 days perioperative morbidity and mortality rate was 0%. Median follow up was 72.5 month (range 5–168 months). Six of ten patients were free of progression until last follow up.

Conclusions

In our experience at the University Clinic in Freiburg Germany, interstitial radiosurgery based on MRI is a safe and effective method to diagnose and treat low grade gliomas of the brain stem. Furthermore randomized studies are needed to confirm the therapeutic impact of this method in comparison to external beam radiation of brain stem gliomas.

224 – Poster presentation

Acute Ischemic Stroke during DBS Surgery of Globus Pallidus Internus: A Rare Complication of Deep Brain Stimulation: Report of 5 Cases

Angela Elizabeth Downes, Nader Pouratian
Tampa, FL, and Los Angeles, CA

Introduction

Deep brain stimulation (DBS) of the globus pallidus internus (GPi) is a clinically proven efficacious treatment for patients with Parkinson's disease (PD) refractory to medical therapy. Several studies have reported several complications associated with DBS surgery, most commonly addressing infection and hemorrhage; however, reports of acute cerebral ischemic infarctions during GPi DBS implantation surgery are rare.

Methods

We present a series of five patients who underwent bilateral GPi DBS lead placement for PD complicated by clinically significant ischemic strokes during surgery. All surgeries were performed with single tracks for both microelectrode recording and macroelectrode placement.

Results

All five patients developed acute onset of lethargy, dysarthria, contralateral facial and/or hemibody weakness during either microelectrode recording or DBS electrode implant. Patients with tremor also experienced an abrupt resolution of contralateral tremor. Immediate postoperative CTs performed in all cases did not reveal any evidence of hemorrhage. MRIs obtained in three patients revealed ischemia in the posterior limb of the internal capsule and lateral putamen.

Conclusions

Ischemic stroke is a rare complication of DBS surgery. The authors present a case series of symptomatic ischemic stroke occurring during DBS placement. The mechanism is not clear, but small vessel vasospasm could have occurred due to direct compression or electrical stimulation. Time of symptom onset was different across patients; therefore, defining a unifying theory remains speculative.

225 – Poster presentation

Staged versus Simultaneous Bilateral Deep Brain Stimulation Surgery for Parkinson's Disease: Impact on Health Outcomes

Terence Verla, Ulysses Toche, Owoicho Adogwa, John Gallis, Yuliya Lokhnygina, Shivanand P. Lad
Durham, NC

Introduction
Deep Brain Stimulation (DBS) has been shown to be effective in treating medically refractory Parkinson's Disease (PD), with long-term improvement in quality of life. Bilateral DBS can be performed simultaneously or staged based on symptom severity. However, controversy exists over the role of simultaneous versus staged-bilateral DBS on outcomes. The goal of this study was to evaluate the impact of staging on health outcomes following DBS for PD.
Methods
A large, retrospective cohort study was performed using the Thomson Reuter's MarketScan® national database, examining patients who underwent bilateral DBS between 2000 and 2009. Patients were separated into cohorts based on simultaneous-bilateral or staged-bilateral DBS. Staged-bilateral was defined as DBS contralateral to the initial procedure, within 90-days and without lead revision or generator placement. Multivariate regression analysis was used to evaluate complications, lead revision, generator reprogramming and annual healthcare cost.
Results
A total of 653 patients were included in the analysis (Simultaneous: 531(81.3%) vs. Staged: 122(18.7%). The mean±SD age was 61.4±9.6years (Simultaneous: 60.9±9.6years vs. Staged: 63.6±9.5years). Overall, 30.6% of patients were female (Simultaneous: 31.5% vs. Staged: 27.1%) and 39.2% had a Charlson score of =1 (Simultaneous: 39.6% vs. Staged: 37.7%). After adjusting for age, gender, Charlson index, insurance, employment status and year of procedure, staged-bilateral DBS was associated with increased odds of device-related complications (OR 1.99; 95% CI 1.21, 3.26; p=0.006), increased postoperative generator reprogramming time (RR 1.15; 95% CI 1.06, 1.25; p<0.001) and lower hazard of lead revision (HR 0.51; 95% CI 0.31, 0.83; p=0.007). There was no significant difference in annual healthcare cost between both cohorts.
Conclusions
In this retrospective analysis, staged-bilateral DBS was associated with increased device-related complications and decreased incidence of lead revision, compared to simultaneous-bilateral DBS. These results may be valuable to physicians and patients in the decision algorithm when planning bilateral DBS for PD.

226 – Poster presentation

Pneumocephalus and Electrode Deviation in Deep Brain Stimulation for Parkinson's Disease

J. Nicole Bentley, Karen Cummings, Kelvin Chou, Parag G. Patil
Ann Arbor, MI

Introduction
Occurrence of brain shift during deep brain stimulation (DBS) may lead to deviation in electrode placement, which may reduce clinical benefit. Intracranial air (ICA) has been cited as one potential factor influencing the amount of shift. We analyzed a series of patients with ICA after DBS to better understand the impact on electrode position and clinical outcomes.
Methods
We performed a retrospective review of patients treated at our institution for refractory PD who underwent bilateral STN DBS. The immediate post-operative CT was fused with the 4-week follow-up CT, and deviation of the electrode was determined. Amounts of ICA were calculated and correlated to various parameters. Patients were grouped according to amount of ICA, and clinical outcomes were assessed for each of these groups.
Results
ICA had resolved fully at follow-up. In 60 total leads, average deviation at the tip was 1.14 ± 0.72 mm. The proximal lead deviated anteriorly an average of 2.97 ± 1.81 mm. Mean ICA was 20.7 ± 13.5 cm^3, and did not significantly correlate to duration of disease, but did correlate to patient age and total number of passes ($p < .05$). There was a statistically significant correlation of ICA to proximal lead deviation (Pearson's test, $r=.356$, $p = .03$), but not to tip deviation. Patients in group 4 with ICA greater than 30 cm^3 had worse scores on the MDS-UPDRS part 3 at 6 and 12 months, while those with <30 cm^3 had scores that were comparable and stable across time.
Conclusions
Regardless of the amount of ICA introduced during surgery, electrode deviation at the tip is minimal. With ICA <30 cm^3, there appears to be a negligible effect on clinical outcome scores, however, ICA greater than this may play a role in DBS success. Further studies with larger numbers of patients are needed to fully examine this.

227 – Poster presentation

The Role of Intra-Operative Neurophysiological Monitoring (IOM) ,fMRI and DTI in the Resection of Lesions in the Supplementary Motor Area (SMA)

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Liverpool, United Kingdom

Introduction

Resection of lesions in the SMA (LGG, HGG, CD or cavernoma) have been historically challenging due to the relatively high incidence of temporary/permanent SMA syndrome. The advent of fMRI, DTI tractography and the resurgence of IOM have significantly improved the extent of resection in this area and the preservation of neurological function. In this retrospective study we report our experience in the resection of lesions in the SMA with IOM, fMRI/DTI.

Methods

30 patients with LGG/HGG or cavernoma in the SMA were operated in our Institution with IOM and integrated fMRI/DTI over a period of 3 years. There were 15 female and 15 male. 18 patients had lesion in the dominant frontal lobe. 20 Patients presented with seizures , 4 with neurological deficit and 6 with headache. There were 20 LGG, 6 HGG and 4 cavernoma. All patients had fMRI/DTI; neuronavigation was used in all cases. IOM was used in all cases (MEP, subcortical stimulation and direct SMA stimulation) and awake craniotomy was used in selective cases. Post-operative MRI was used to evaluate the extent of resection.

Results

Macroscopic resection was achieved in all cases with no mortality. We found concordance between fMRI/DTI and cortical/subcortical stimulation in all cases. Direct stimulation of the SMA was not associated with any recorded motor response. 2 patients experienced post-operative SMA syndrome with full recovery at 6 months follow up despite normal MEP and subcortical stimulation during resection. Those lesions that extended towards M1 were resected with no deficit post-operatively.

Conclusions

IOM and fMRI/DTI are in our opinion essential in the resection of lesion in the SMA. Although these techniques can prevent permanent neurological deficit and maximize resection, they are not sufficient to prevent/predict the occurrence of SMA syndrome.

228 – Poster presentation

Cost Analysis for MRI guided DBS Electrode Placement

Wendell Bradley Lake
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Introduction

Image guided methods for DBS electrode placement are increasingly common. Both CT guided and MRI guided methods have been proposed as options for patients who are unable to undergo awake surgery. Very little has been written regarding the cost of image-guided functional neurosurgery. With increasing financial pressure on healthcare systems the cost of surgical methods will face increased scrutiny. This study retrospectively compares the cost of DBS electrode placement by MRI guided methods to the cost of placement by awake microelectrode recording.

Methods

DBS electrode placement under MRI guidance was evaluated retrospectively for 10 patients at our home institution. Factors considered in cost analysis were the costs of operating room time, material resources, and the need for revision procedures. The cost of MRI image guided procedures was compared retrospectively with a cohort of patients who underwent awake placement of DBS leads.

Results

Operating room time was found to be a significant factor affecting cost. Material resources were also a significant factor influencing cost. No revision procedures were necessary for the DBS leads placed under image guidance. As more MRI guided procedures were performed total operative time decreased indicating a learning curve phenomenon.

Conclusions

MRI Image guided DBS lead placement is a financially viable option for patient's unable to undergo awake electrode placement. As more MRI guided procedures are performed clinician familiarity improves and this may decrease cost. Additionally, the cost of material resources required for MRI guided electrode placement may decrease as the technology becomes more common. These changes may further improve the economic viability of this technology.

229 – Poster presentation

Stimulation of the Motor Cortex for Chronic Neuropathic Pain: Anatomo- Clinical Correlations

Afif Mohammad Afif, Patrick Mertens
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Introduction

The aim of this study was to locate the electrode contacts implanted over the cortex and to search the relationship between the anatomical location and the analgesic effect of each contact.

Methods

22 patients suffering from central and / or peripheral neuropathic pain were implanted with stimulation of the precentral cortex. The implantation of the electrodes was performed using intraoperative: 1) Anatomical identification by Neuronavigation with 3D MRI, 2) Somesthetic evoked potentials monitoring to check the potential reversal over the central sulcus, 3) Electrical stimulations to identify the motor responses and its somatotopy. In order to locate the electrodes postoperatively, a 3D-CT was performed in each case and fused with the preoperative MRI. The clinical analgesic effects of cortical stimulation were collected on a regular basis (VAS reduction > 50%, drugs consumption). Data were analyzed to search a correlation between the anatomical position of contacts and analgesic effects.

Results

Post implantation analgesic effects were obtained in 19 patients out of 22. The analgesic effect was accompanied by reduction of the drugs consumption in 17 patients . The post-operative 3 D CT analysis shows a correspondence between the effective contacts localization and the motor cerebral cortex somatotopy in the patients with post-operative good analgesic effects. The contacts with the best analgesic effects were localized over the central sulcus. No correspondence was found between the contacts localization and the motor cerebral cortex somatotopy in the 3 patients with no analgesic effects. In two out of these three patients, analgesic effects were obtained after a new surgery was done changing the electrode position based on the motor cortex somatotopy corresponding to the painful area.

Conclusions

This study shows the correlation between position of the contact over the precentral cortex and the analgesia obtained when somatotopy of the stimulated cortex corresponds to the painful area.

230 – Poster presentation

Mathematical Equation for Standardized Burr Hole Placement in Stereotactic Lead Placement for Deep Brain Stimulator to Minimize the Risk of Complications

Timur M. Urakov, Jonathan R. Jagid
Miami, FL

Introduction

Stereotactically guided lead placement for deep brain stimulation requires a carefully planned out trajectory and approach. Point of entry at the cortex is usually selected to be over a gyrus avoiding veins. The angle of lead entry into the skull is different from the perpendicular direction of burr drill. If the burr hole is not placed properly the inner plate of skull may be in a way of the lead trajectory, which creates a snowball effect of complications from trajectory readjustment to improperly fitting hardware.

Methods

The trigonometric principles were applied to the set up of stereotactic lead insertion in order to elucidate a mathematical equation that would predict precise position of the burr hole in order for the lead to enter exactly in the middle of the opening at the dural level. Further, twenty DBS patients were reviewed retrospectively in order to elucidate which variables of the equation (angle of lead entry, angle of skull plate, and skull thickness) could be safely generalized for all patients.

Results

The resulting equation, that will be presented, is a function of tangent dependent on skull thickness and the two angles mentioned above. Patient population review showed that the variable may be generalized, however individual application of the equation is more likely to produce favorable results.

Conclusions

This new mathematical equation allows for precise determination of burr hole placement and reduces operator-dependent variability. The equation may be integrated into current navigation software improving precision and safety of the lead placement in DBS surgery. Findings could further be extrapolated to all stereotactic procedures requiring a burr hole for approach.

231 – Poster presentation

Prospective Investigation of Peripheral Nerve Stimulation Functional Outcomes in Chronic Pain Patients

Priscilla De La Cruz, Joannalee C. Campbell, Meghan Wilock, Jessica Haller, Steven G Roth, Elaina Pullano, Julie G. Pilitsis
Albany, NY

Introduction
Peripheral Nerve Stimulation (PNS) is an off-label use of an FDA approved device that has been shown in case series to be efficacious for chronic facial neuropathic pain. Patients selected for PNS have pain symptoms refractory to best medical treatment. We present prospective data on PNS outcomes on quality of life and depression.
Methods
Nine patients with occipital neuralgia (n=2), trigeminal neuropathic pain (n=1), and migraine (n= 6) were implanted with PNS after a trial with a 50% or greater improvement in pain. All patients completed the Oswestry Disability Index (ODI), Beck Depression Index (BDI), and Pain Catastrophizing Scale (PCS) prior to implantation and at most recent follow-up (mean= 4.3 months). Data was analyzed using one way ANOVA.
Results
At most recent follow up of 9 patients BDI improved from 16.6 to 9.8 (p=0.01) and PCS improved from 32.8 to 18.5 (p=0.006). Improvement in quality of life became apparent at six months (n=4) with a significant improvement in ODI from 43.2 to 28.0 (p=0.035).
Conclusions
This prospective study demonstrates that PNS for craniofacial neuropathic pain improves depression and quality of life measures in short term follow up.

232 – Poster presentation

Cervical Spinal Cord Stimulation For Prevention and Treatment of Cerebral Vasospasm: Long-Term Follow Up Data

P. Hari Krishna, Siddharth Vannemreddy, Vyas Viswanathan, Konstantin V. Slavin
Chicago, IL

Introduction
Several years ago we hypothesized that prolonged cervical spinal cord stimulation (cSCS) in the acute settings of aneurysmal subarachnoid hemorrhage (aSAH) may be used to prevent and/or treat arterial vasospasm. To prove this, we performed a prospective study of cSCS in a small group of aSAH patients with main goal to evaluate its clinical effects, and to establish feasibility and safety of this neuromodulation modality in this complicated patient population. Initial results were encouraging but the long-term outcome remains to be determined.
Methods
Single-arm non-randomized study of cSCS in aSAH involved percutaneous implantation of 8-contact electrode in 12 consecutive aSAH patients that satisfied strict inclusion criteria. All patients were stimulated for 14 consecutive days or until discharge while monitoring for clinical and angiographic vasospasm. The study was conducted in 2009 and initial results were presented soon thereafter. Patients have been followed for 4 years at regular intervals with outcome data prospectively collected and analyzed.
Results
Mean age of 12 patients was 49 years (range 27-62); average Hunt & Hess grade was 2.9 (range 2-4) and Fisher grade was 3.3 (range 2-4). Three were coiled and 9 were clipped. Angiographic vasospasm occurred in 6/12 patients and clinical vasospasm in 2/12. No patients showed any vasospasm-related neurological complications. The patients recovery was followed through the Modified Rankin Scale and the Glasgow Outcome Scale with a mean of 2.1 (range 1-6) and 6.6 (range 1-8) respectively.
Conclusions
The first North American study for prevention of vasospasm after aSAH conclusively showed both safety and feasibility of this promising treatment approach. Long term follow up revealed no adverse effects of cervical SCS in this patient category. Based on these results, a larger multi-center study of cSCS in aSAH will be the next step in evaluation of clinical effectiveness comparing active arm to a matched control group.

233 – Poster presentation

Deep Brain Stimulation for Refractory Tourette syndrome: Analysis of Centromedian/Parafasicular Target with Symptom Improvement

Richard S. Dowd, Michael Pourfar, Nrupen Baxi, Alon Y. Mogilner
New York, NY

Introduction
Tourette syndrome (TS) is a complex neuropsychiatric disorder characterized by multiple motor and phonic tics. While pharmacological and behavioral therapy can be effective in most patients, there is a subset of patients who remain refractory with few other options. Increasing clinical evidence from multiple centers suggests that deep brain stimulation (DBS) can be effective in refractory TS patients. Currently, there are reports of 9 different targets being used with DBS for TS, thus the roadblocks to its success include questions not only of efficacy, but of optimal target selection.
Methods
6 patients with refractory TS underwent DBS of the centromedian thalamus by our team over a five-year period. Patients were evaluated by a multidisciplinary team, with preoperative objective assessments including the Yale Global Tic Severity Scale (YGTSS) and Yale-Brown Obsessive Compulsive Scale (YBOCS). YGTSS scores were calculated at visits immediately post-operatively and at their latest follow-up. Coordinates of the active DBS contacts were calculated and projected onto the patient's pre- and post-operative imaging.
Results
Patients showed a decrease of 57% (Z=-2.021; p=0.028) in the total tic severity at their immediate post-operative visit. At their last visit, their scores maintained the improvement, decreasing from pre-operative scores by 55% (Z=-2.021; p=0.028). The average position of the active contact relative to the midcommissural plane was 6.4 mm lateral, 2.6 mm posterior and 1.6 mm superior on the left, and 6.3 mm lateral, 2.1 mm posterior, and 2.6 mm superior on the right. There were no long-term complications. One patient suffered an extension lead fracture, necessitating unilateral revision and temporary removal for infection, followed by replacement.
Conclusions
Our data adds to the growing body of literature suggesting that DBS of the CM-Pf thalamus is effective in the treatment of refractory TS. The active contacts localize to the anterior CM-Pf / posterior VOi / Vom region.

234 – Poster presentation

Validation of Intraoperative 32-Slice Computed Tomography as a Useful Adjunctto MR- and MER-Guided DBS Implantation in STN-Targeted Parkinson's Disease: Exciting Prospects on the Horizon

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Irvine, CA, and San Diego, CA

Introduction
The STN is the most common target for motor-predominant PD. We are unaware of any comparative studies on a cohort utilizing all of modern modalities, namely intraoperative 32-slice CT, preoperative MR, macrostimulation, and MER-guided DBS implantation. We attempt to describe the contribution of each to clinical outcome, arriving at the surprising conclusion below.
Methods
Preoperative and postoperative clinical results were quantified. Patients had a pre-operative 1.5/3T MRI, were then induced and placed in a stereotactic frame. Neurologica BodyTom was then used to scan the patient. Atlas-derived target was calculated and final targeting was determined by MER/macrostimulation data.
Results
A significant improvement in quality of life was experienced. MER influenced changes in indirect target coordinates. Given a lead diameter of 1.75 mm, and an inter-microelectrode distance of 2 mm, this brought about the tantalizing question of whether or not we could use this system to directly target the STN. We had a blinded neuroradiologist select an ideal target using our paradigm. In doing so, the range from target decreased ty only 1.08 to 2.19 mm. Given the robust clinical outcomes we obtained with the ranges outlined above and the deviations listed in presentation, this study portends the exciting possibility of directly targeting the STN via high resolution MRI and potentially eliminating the need of MER.
Conclusions
Though we are conducting ongoing studies to verify this hypothesis, the use of our intraoperative scanner has resulted in nearly 90% of patients experiencing symptomatic relief. We encountered no hemorrhages, strokes, or infections, and only 3 lead position changes, all done intraoperatively. This technique is an exciting improvement regardless of targeting implications.

235 – Poster presentation

The Impact of Sacral Nerve Stimulation in Treatment of Urinary and Fecal Incontinence

Angelo Lavano, Giorgio Volpentesta, Marisa De Rose, Giusy Guzzi, Giuseppe Vescio, Francesco Lavano, Federica Deodato, Attilio Della Torre
Catanzaro, Italy

Introduction

Our aim is to investigate therapeutic value of sacral neuromodulation with dorsal transforamenal tined leads implantation as method of treatment of urinary and fecal incontinence.

Methods

We selected 23 patients: 16 patients had urinary incontinence, 5 mixed urinary/fecal incontinence and 2 fecal incontinence. All underwent preliminary urodynamic and anorectal investigation. 60% had hyperreflexia-dyssinergia, 35% hyperreflexia, 5% dyssinergia. Patients with fecal incontinence had all positive rectal manometry. SNS tined leads were placed percutaneously with transforamenal dorsal approach in S3 foramen on all 23 patients; in 11 cases implant was bilateral.

Results

In urinary incontinence-urgency at 12 months follow-up we obtained excellent and good clinical results on urinary losses/day in 13 of 14 patients with increase in voided volumes, volume voided/void and reduction of degree of urgency. In mixed incontinence there was decrease of urinary leakages/day in 4 patients and mean values of episodes fecal incontinence/week and fecal urgency/week significatively decreased. In fecal incontinence there was significant reduction of episodes of fecal incontinence/week and fecal urgency/week. QoL (SF-36) was significantly improved. Mean available follow-up was 30 months (6-48); results remained satisfactory but adjustments of stimulation parameters were necessary. The complications rate was 12% (4 cases): 1 case of lead displacements in presacral space (change in lead contacts polarity), 1 case of lead fracture (implant of new lead), 1 case of superficial wound dehiscence and 1 case of infection.

Conclusions

SNS effectively provides long-term benefits for patients with drugs resistant sphinteric troubles and improves both patients' level of independency and QoL. It is a safe therapeutic method with simple procedure and relatively low complication rate. Major technological advancement, like use of "tined lead", allows wide application of SNS with high success rate, reducing lead migration. Bilateral lead implantation improves the effectiveness (neurogenic origin).

236 – Poster presentation

Demographic, Clinical and Surgical Predictors of Response to Thalamic Stimulation for Tremor Disorders

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Toronto, Ontario, Canada

Introduction

Ventralis intermedius thalamic deep brain stimulation (Vim DBS) for medication-refractory tremors has been shown to greatly improve severity of limb tremor in several case series although a significant variability in the outcomes as well as a decline in benefit over time (secondary failures) have been found. No study has investigated the predictors of the outcome.

Methods

In this retrospective single center study, we collected the demographic, clinical (diagnosis, response to medications, tremor rating scores, familiarity) and surgical (side, microlesional effect, active contact(s) coordinates, stimulation parameters) features of all the tremor patients who underwent Vim DBS in the period between 1994-2014.

Results

We collected 65 cases (45.6% essential tremor,11.8% multiple sclerosis, 13.2% parkinsonian, 11.8% other etiologies). Mean age at time of surgery is 60.6±13.5 years, 38% are females and 44% are males, mean follow-up duration after surgery is 43.7 ± 47.8 months, the mean tremor score was 20.75± 5 at baseline, 10.57±6.85 at 1 year and 14.04±8.26 at last follow up. At 1 year, comparing the group with a good response (defined as 50% reduction in tremor) to the group with poor outcome, there was no statistically significant difference in gender, diagnosis, response to alcohol, duration of disease or pre-operative tremor scores. However, at last follow up, the group with good outcome has more essential tremor cases and good response to alcohol with p values of 0.005 and 0.035 respectively. In the whole group, 13.2% of patients had a failure of response at 1 year compared to 32.4% at the last follow up

Conclusions

The outcome of tremor reduction after Vim DBS is highly variable, major factors explaining such variability were diagnosis and response to alcohol. These features should be taken into account during the pre-operative selection of patients.

237 – Poster presentation

Impact of Advancing Age on Outcomes of Deep Brain Stimulation for Essential Tremor

Terence Verla, Owoicho Adogwa, John Gallis, Yuliya Lokhnygina, Beth Parente, Patrick Hickey, Dennis A. Turner, Shivanand P. Lad
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Introduction
Essential tremor (ET) was the original indication for Deep Brain Stimulation (DBS), with FDA-approval since 1997. Given that the prevalence of ET increases nearly 10-fold with age, we evaluated the step-wise impact of increasing age on short-term complications following DBS surgery. We hypothesized that increasing age would be associated with an increase in postoperative complications.
Methods
A large retrospective cohort study was performed using the Thomson Reuters MarketScan® national database, examining patients who underwent DBS for ET from 2000-2009. Hospital length of stay, and aggregate and individual complications within 90 days following surgery were evaluated. Multivariate logistic regression analysis was used to calculate complication odds ratios for each 5 year age epoch after controlling for covariates.
Results
A total of 661 patients were included in the analysis. The mean (SD) patient age was 61.9 (14.3) years, with 17% of individuals age 75 or older. Overall, 56.9% of patients were male, and 44.6% had a Charlson Comorbidity Score of one or greater. 7.1% of patients experienced at least one complication within 90 days, including wound infections (3.0%), pneumonia (2.4%), hemorrhage or hematoma (1.5%), or pulmonary embolism (0.6%). After adjusting for covariates, increasing age ranging from <50 to 90 years, did not significantly impact overall 90-day complication rates (OR 0.89 per 5-year increase; 95%CI 0.77, 1.02; p=0.102). The two most common procedure-related complications, hemorrhage and infection, did not significantly increase with age (hemorrhage: OR 1.02; 95%CI 0.77, 1.37; p=0.873, infection: OR 0.88; 95%CI 0.72, 1.07; p=0.203).
Conclusions
Among older ET patients, 90-day complication risk and the risk of postoperative hemorrhage or infection remained relatively stable, despite increasing age. Our findings suggest that age should not be a primary exclusion factor for determining candidacy for DBS and possible expansion of the traditional therapeutic window.

238 – Poster presentation

Why Does Deep Brain Stimulation Do the Same Thing in the STN and GPI? A Computational Study of Deep Brain Stimulation in the Basal Ganglia

Michael Chary, Brian H. Kopell
New York, NY

Introduction
Deep brain stimulation (DBS) is an effective treatment for Parkinson's disease, even though the biological basis for its efficacy is unclear. Stimulation of the subthalamic nucleus and internal segment of the globus pallidus lead to equivalent symptomatic relief. Here we present a computational model of the basal ganglia to understand why similar stimulation patterns in glutamatergic and GABAergic nuclei produce equivalent effects.
Methods
We simulated the activity of six homogeneous neuronal populations, connected according to the consensus macrocircuitry for the basal ganglia using the formalism of a Hopfield net. The six neuronal populations represented the (1) cerebral cortex, (2) striatum, (3) internal segment of the globus pallidus and pars reticulata of the substantia nigra, (4) subthalamic nucleus, (5) external segment of the globus pallidus, and (6) thalamus. The simulations accounted for only linear pairwise interactions between nuclei, ignoring plasticity and higher-order correlations.
Results
Short square pulses of current (high-frequency stimulation) produce equivalent effects in the subthalamic nucleus and internal segment of the globus pallidus. Patterns of stimulation in the internal segment of the globus pallidus with long current pulses and brief inter-pulse intervals are more effective at decreasing thalamic activity than those in the subthalamic nucleus.
Conclusions
Our results suggest that the pattern of stimulation could be tailored in different nuclei to target different types of Parkinson's. Our model can be extended to other brain regions, such as the mesolimbic system, to identify novel target nuclei based on the functional equivalence of those nuclei to known sites. More generally, an exploration of different patterns of stimulation in different parts of the basal ganglia may lead to a deeper understanding of the basis of deep brain stimulation.

120: Monday, June 2, 2014, 2:30-2:40 pm; PS #3
Subthalamic Nucleus Deep Brain Stimulation Induces Motor Network BOLD Activation

Paul Hoon-Ki Min, Erika K. Ross, Kendall Dennis, Ju Ho Jeong, Bryan Striemer, Joel Felmlee, Su Youne Chang, Kevin Bennet, Kendall H. Lee
Rochester, MN

Introduction
Approximately 100 000 patients with neurologic and neuropsychiatric disorders, including PD, have been successfully implanted with DBS systems worldwide. Although the mechanism of DBS is not completely understood, it is known that modulation of brain function depends on precise targeting and stimulation of specific anatomical sites within complex neural circuits. Functional magnetic resonance imaging (fMRI) is a powerful method for identifying network activation evoked by DBS with high temporal and spatial precision. Here, we test the hypothesis that the modulatory effect observed with subthalamic nucleus (STN) DBS is, at least in part, due to activation of both motor and non-motor circuitry using fMRI.
Methods
An in-house developed MR image-guided stereotactic targeting system delivered a mini-DBS stimulating electrode, and we identified specific changes in global network activation during STN DBS in healthy rhesus macaques (n=2) by combining fMRI with a normalized functional activation map and general linear modeling.
Results
Our results show that STN DBS significantly increased blood oxygenation level-dependent (BOLD) activation in the ipsilateral sensorimotor cortex, caudate nucleus, pedunculopontine nucleus, cingulate, insular cortex, and in contralateral cerebellum (FDR < 0.001). The region of interest (ROI) analysis showed delayed hemodynamics peaking at 8s~14s after stimulation, where the ipsilateral primary motor cortex and bilateral cingulate cortex showed initial decreased pattern in the BOLD change.
Conclusions
Our results demonstrate that STN DBS evokes neural network grouping within the motor network and the basal ganglia and highlight the importance and specificity of their neural circuitry activation patterns and functional connectivity. These results highlight the importance of global network activation as a potential mechanism leading to clinical therapeutic outcome in DBS patients.

122: Monday, June 2, 2014, 2:50-3:00 pm; PS #3
Patient-specific Anatomical Model for DBS Surgery Derived by 7T MRI

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Minneapolis, MN, and St. Paul, MN

Introduction
Current standard clinical imaging protocols do not have sufficient resolution and/or SNR to delineate brain structures relevant to deep brain stimulation (DBS) surgery. Structural images acquired at 7 Tesla (T) exhibit rich informational content with potential utility for clinical applications. Here we utilized 7T images to create patient-specific anatomical models to enhance pre-surgical DBS targeting as well as post-surgical visualization of the DBS lead position and orientation, including its four individual contacts.
Methods
Seventeen candidates for DBS surgery were scanned preoperatively on standard clinical 1.5T and 7T MRI systems. Segmentations and 3D volume rendering of the anatomical target (GPi or STN) and adjacent structures were generated based on susceptibility-weighted images (SWI) and T2-weighted images acquired at 7T. Serial microelectrode recording (MER) techniques were used to map the target region and optimize DBS placement. A postoperative CT was obtained and co-registered to the preoperative 7T MRI. The registered images were then used to assess electrode and intraoperative microelectrode locations relative to the 3D anatomical model and compared with MER mapping and clinical programming data.
Results
A patient-specific anatomical model depicting the DBS target and surroundings structures was created for each patient. The data indicates excellent agreement between the 3D model of DBS targets, the MER mapping and the post-operative electrode programing configuration.
Conclusions
Structural 7T MRI can be used to create accurate, patient-specific models for use in DBS procedures. Specifically, these models may be of use to (1) visualize the intended structures for direct targeting; (2) verify final DBS lead location, including individual stimulation contacts, post-surgery; (3) guide and facilitate initial DBS programming for maximum benefit to the patient; and (4) allow for further understanding of the optimal location of the DBS electrode within the target region. These new capabilities will enhance and improve DBS outcomes.

145: Tuesday, June 3, 2014, 10:35-10:45 am; PS #6

Interventional Magnetic Resonance Imaging (iMRI)-Guided Delivery of Therapeutics into the Brain with Radially Branched Deployment (RBD)

Matthew Silvestrini, Dali Yin, Alastair Martin, Valerie Coppes, Preeti Mann, Nalin Gupta, Scott Panter, Xianmin Zeng, Paul Larson, Philip A. Starr, Tejal Desai, Daniel A. Lim
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Introduction
Intracerebral cell transplantation, gene therapy, and drug infusions are being pursued for as treatments for many neurological diseases, and effective therapeutic delivery is critical for clinical success. Currently, most intracranial therapeutic delivery is performed with straight cannulas inserted with indirect stereotactic targeting. Radially branched deployment (RBD) of a catheter at multiple points along the initial cannula penetration tract facilitates therapeutic distribution. Interventional magnetic resonance imaging (iMRI) enables real-time monitoring of stereotactic procedures and could be advantageous for RBD. Our objective was to develop an iMRI-guided RBD platform for intracerebral procedures.
Methods
We constructed an RBD system with FDA-approved, MRI-compatible materials. Precision of catheter deployment was assessed in an agarose brain mimic. With iMRI-guided RBD, superparamagnetic iron oxide (SPIO) beads were delivered to the striatum of live swine and to the putamen of human cadavers. Human embryonic stem cell-derived dopaminergic (hDA) neurons were delivered to the swine striatum. RBD was also tested for the delivery of a convection-enhanced delivery (CED) catheter both in brain mimic and swine brain with iMRI-guidance.
Results
Our iMRI-guded RBD system functioned as an "add-on" to the ClearPoint stereotactic platform and software. Catheter deployment was continuously variable up to 12mm radial and precise. Multiple SPIO deposits were delivered into the swine striatum without incurring neurological deficits, and coverage of the human putamen could be achieved with a single initial cannula insertion. hDA neurons were biocompatible and successfully delivered to multiple locations in the swine striatum. RBD enabled CED delivery to multiple brain locations via a single guide cannula insertion.
Conclusions
iMRI-guided RBD overcomes some of the technical limitations inherent to the use of straight cannulas and indirect stereotactic targeting. This neurosurgical device and approach may facilitate clinical trials involving intracerebral cell transplantation, gene therapy, and drug infusions.

147: Tuesday, June 3, 2014, 10:55-11:05 am; PS #6

Development of High Precision MRI Guided Stereotactic System for Nonhuman Primate

Ju Ho Jeong, Paul Hoon-Ki Min, Erika K. Ross, Kendall H. Lee, Kendall Dennis, Seong Rok Han, Michael P. Marsh, Bryan Striemer, Joel Felmlee, Stephan Goerss, Su-Youne Chang, Kevin Bennet
Rochester, MN

Introduction
Existing methodologies for stereotactic neurosurgery in non-human primate (NHP) models are somewhat limited and are not optimized to the characteristic neuroanatomy of NHP. So we have developed a customized MRI guided stereotactic system for NHP to facilitate implantation accuracy. The in-house NHP stereotactic head frame and the add-on systems were designed similarly to the devices for the human functional surgeries and were modified for the NHP DBS model.
Methods
The specifications of our stereotactic system were developed with reference to other popular stereotactic systems, including KOPF®, Cicerone®, microTargeting Platform®, Leksell®, and CRW® system. It was designed with six degrees of freedom in alignment. The arc, head frame and fixator, localizer box, and immobilizer were designed to fit NHP and to have full MRI compatibility with decreased distortion. The MRI coil is custom-built and integrated in localizer box for higher quality images during targeting and fMRI study. The customized targeting program was developed and verified with phantom study. Preparatory mockup models were made with a 3D printer. The final version was fabricated according to amended design. The head frame was mechanically calibrated with reference point (Frankfurt zero). The parameters in MR imaging sequence were optimized in order to minimize the distortion. Finally the errors were measured in coordinates using a stereotactic phantom with nine targeting points to confirm accuracy.
Results
The customized MRI guided stereotactic system for nonhuman primate showed sub-millimeter target accuracy with high quality anatomical/targeting MR images and fMRI data
Conclusions
We developed a modified stereotactic arc system, custom-built MRI coil, and targeting program for NHP brain. This system will provide an accurate and customized platform to investigate the underlying mechanism of DBS in NHP models through stereotactic and functional studies.

148: Tuesday, June 3, 2014, 11:05-11:15 am; PS #6

Stereotactic Technique Determines Accuracy and Efficiency in "Asleep" DBS

Zaman Mirzadeh, Kristina Chapple, Meg Lambert, Rohit Dhall, Francisco A. Ponce
Phoenix, AZ

Introduction
Advances in neuroimaging and surgical navigation have led surgeons to consider performing deep brain stimulation (DBS) surgery under general anesthesia. Compared with traditional DBS technique, where targeting is refined by intraoperative electrophysiology and test stimulation, the endpoint of so-called "asleep" DBS is stereotactic accuracy. We present our results performing asleep DBS with comparison to traditional DBS.
Methods
For both asleep and awake procedures, direct targeting was performed on preoperative MR images, which were subsequently fused with intraoperative CT images for stereotactic registration. Leads were placed using either a frameless or frame-based stereotaxy. Following lead placement, CT images were obtained intraoperatively to determine accuracy.
Results
188 patients (n=95 awake, n=93 asleep; mean age 62) had 345 leads placed (179 GPi, 56 STN, 87 VIM) over a 2-year period. Deviation from the planned trajectory (radial error) was compared between patients who underwent asleep DBS and awake DBS. Leads placed in asleep patients had significantly less radial error than those placed with a single pass in awake patients (0.9 mm [175 leads] vs. 1.4 mm [105 leads]; $p<0.001$). For the asleep cohort, the mean vector error was 1.2±0.7 mm, with a significant difference between frame and frameless stereotaxy (Leksell: 1.1 mm [101 leads] vs. Nexframe: 1.3 mm [74 leads], $p=0.028$). A significant difference between frame and frameless cases was also evident in both case time (Leksell: 2.0 hrs vs. Nexframe: 2.5 hrs; $p=0.004$) and operating room time (Leksell: 3.1 hrs vs. Nexframe: 4.2 hrs; $p<0.001$).
Conclusions
In our experience, asleep DBS resulted in smaller stereotactic error over single pass awake DBS, and frame-based stereotaxy outperformed frameless stereotaxy with regard to accuracy, surgical time, and operating room time.

149: Tuesday, June 3, 2014, 11:15-11:25 am; PS #6

Evaluation of Tumor Progression and Detection of New Tumors during Repeat Stereotactic Radiosurgery for Brain Metastases Utilizing a Co-registration Imaging Tool

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Pittsburgh, PA

Introduction
Repeat stereotactic radiosurgery (SRS) procedures are becoming common place, especially for the management of brain metastases. It is important to correctly identify tumors that require treatment at the time of repeat SRS and it can be challenging to distinguish between successfully treated tumors, tumors that have progressed, and new tumors. The objective of this report was to explore the feasibility of a new co-registration technique to identify tumors requiring treatment at repeat SRS.
Methods
Ten patients who underwent repeat SRS for brain metastases were identified. The contrast-enhanced volumetric T1-weighted magnetic resonance images (MRI) obtained during the previous SRS were co-registered with the new MRI images and the resulting two-color format image was used to evaluate the status of visualized tumors.
Results
Using the two-color co-registered images, tumors could be characterized as either: resolved, regressed, stable, progressed, or new. Two-hundred seven tumors were identified. Overall, 12.6% of tumors completely resolved, 24.2% showed regression, 12.1% remained stable, while 7.2% showed growth. Fourty-four percent of the tumors identified were new.
Conclusions
This co-registration technique makes clinically relevant changes conspicuous on MRI at the time of repeat SRS. It distinguishes between tumors requiring treatment (new or progressed) and those that have been successfully treated (regressed or completely resolved). This technique can be used with tumors other than metastases that might require a repeat treatment and can be useful to evaluate tumor response at patient follow up.

151: Tuesday, June 3, 2014, 11:35-11:45 am; PS #6

Reliability of Diffusion-tractography-based Thalamic Segmentation for Identifying Targets for Noninvasive Neuromodulation using MR-guided Focused Ultrasound

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Introduction
While noninvasive modalities like MR-guided focused ultrasound and radiosurgery may provide opportunities for neuromodulation, the success and risk profile will ultimately depend on optimizing targeting. Diffusion tractography based thalamic segmentation has previously been shown to be a reliable method for identifying final targets in invasive neuromodulation, namely deep brain stimulation. The objective of this study was to investigate the role of tractography-based thalamic segmentation for noninvasive neuromodulation, evaluating final MRgFUS thalamotomy sites with that predicted by the proposed imaging technique. This analysis has potential significant implications for noninvasive neuromodulation.
Methods
Fifteen patients with medically refractory essential tremor who underwent MRgFUS generated thalamotomy (ExAblate InSightec) at the University of Virginia Health System were studied. Targeting was performed using indirect targeting methodologies on baseline T1-weighted MR images obtained in all patients. The authors retrospectively performed image analysis for each patient comparing the final thalamotomy location with the predicted optimal site based connectivity-based thalamic segmentation.
Results
Fifteen unilateral thalamotomies were performed with MRgFUS using indirect targeting. The location of the thalamotomy had a high degree of colocalization to the site predicted by connectivity-based segmentation.
Conclusions
This report demonstrates the patient-specific reliability of diffusion tractography based thalamic segmentation to predict final target thalamotomies generated by MRgFUS in the treatment of tremor. This imaging technique can be utilized in other noninvasive modalities such as stereotactic radiosurgery to create targets in neuromodulation that are both accurate and precise as well as specific to the patient's anatomic variations.

239 – Poster presentation

Influence of Radiation Dose to the Outcomes of Gamma Knife Treatment for Trigeminal Neuralgia: A Multi-Factor Analysis

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Sichuan, China

Introduction
Although Gamma Knife radiosurgery (GKR) represents an effective treatment option for trigeminal neuralgia, there is no agreement on the most appropriate treatment protocol. As important factors of the protocol, the radiation variables might significantly influence the outcomes of the treatment. These variables include ideal isocenter location, optimum irradiated nerve length, treatment volume and maximal radiation dose.
Methods
Seventy-three patients with refractory trigeminal neuralgia treated by a maximum doses of 75-90 Gy using either one (n=41) or two (n=32) isocenters were intensively followed up. Using the Gamma-Plan system, the integrated dose delivered to the trigeminal nerve root within the prepontine cistern and the nerve root volume were calculated. Relationships between the clinical outcomes and the radiation variables were statistically analyzed.
Results
At the last follow-up, 21 patients (28.8%), 22 patients (30.1%), 19 patients (26%), 6 patients (8.2%) and 5 patients (6.8%) had grade I-V pain outcomes respectively, and the average mean dose delivered to the trigeminal nerve root, average integrated dose (mJ)and nerve root volume in prepontine cistern were 45.29 Gy, 4.26 mJ and 98.47 mm^3 respectively. The pain relief rate was not significantly improved by a higher amount of integrated dose received by the trigeminal nerve root in prepontine cistern, however, incidence of trigeminal nerve toxicity might be increased (p=0.005).
Conclusions
Our limited results suggested that a higher integrated dose may increase incidence of trigeminal nerve toxicity with no significant benefits in pain relief when the maximal doses were within 75-90 Gy. The protocol of increasing in radiation variables such as longer nerve exposure length and higher maximal dose is not recommended as a routine approach. However, more randomized studies with large number of cases should be carried out to verify the best treatment strategy of GKR for TN.

240 – Poster presentation

The Cerebello-Thalamo-Premotor Cortex Fiber Tract in the Thalamus as an Optimal Target for the Suppression of Tremors

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Introduction

The ventralis intermedius (Vim) nucleus has been targeted for suppression of intractable tremors for many years. However, recently, it has been reported that the ventro-oralis posterior nucleus (Vop) or the posterior subthalamic area (PSA) might be useful alternative targets. These nuclei are not distinguishable by conventional imaging modalities. Now, however, a modality to distinguish them is expected. With diffusion tensor imaging (DTI)-based fiber tractography (FT), some individual fiber tracts in the ventrolateral thalamus can be visualized. The purpose of this study was to show which fibers make the optimal targets in the thalamus for tremor suppression based on DTI-FT.

Methods

Six patients with intractable essential tremor received stereotactic surgeries. Preoperative DTI was performed in all cases. First, four fiber tracts around the ventrolateral neclei of the thalamus were drawn (cerebello-thalamo-premotor cortex, cerebello-thalamo-primary motor cortex, spino-thalamo-somatosensory cortex, and pyramidal tract). Then, active contacts and coagulation sites were confirmed by making fusion images of preoperative DTI-FT and postoperative CT or MRI. Tremor was estimated with the Fahn-Tolosa-Marin (FTM) tremor rating scale preoperatively and postoperatively. Adverse effects after surgeries were also estimated.

Results

FTM tremor rating scale scores were decreased by over 75% in all cases. There were no perioperative adverse effects. Active contacts and coagulation sites were placed on the cerebello-thalamo-premotor cortex fiber tract in all cases.

Conclusions

The cerebello-thalamo-premotor cortex fiber tract might be an optimal target in the thalamus for tremor suppression.

241 – Poster presentation

LINAC Radiosurgery in the Management of Parasagittal Meningiomas

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Haifa, Israel, and Tel Hashomer, Israel

Introduction

At present, there is no general agreement for the best approach to parasagittal meningiomas. Invasion of the superior sagittal sinus is frequent and responsible for relatively high recurrence rates following conventional microsurgery. Radiosurgery has the potential to treat less accessible portions of these tumors and its application in this pathology is increasing both as a primary or a complementary therapeutic tool. Our objective was to evaluate our results with LINAC radiosurgery for treatment of parasagittal meningiomas.

Methods

The patient cohort consisted of 74 patients treated for parasagittal meningiomas by LINAC radiosurgery at the Sheba Medical Center Radiosurgery Unit during a 15-year period. Women accounted for 61% of patients. Thirteen patients (18%) underwent radiosurgery as the primary treatment for their meningioma.

Results

The overall control rate was 90.6% at a mean follow up of 49 months. In 17 patients (22.9%) there was no volumetric change. Fifty patients (67.5%) showed tumor shrinkage ranging from 15-80% of the original mass. In 7 patients tumor recurrence was observed at an average time of 42.2 months after radiosurgery. All the patients with previously untreated tumors were controlled. Symptomatic transient peritumoral edema developed in 5 patients (6.7%) at a mean of 6.4 months after radiosurgery. Three patients complained of protracted headaches post treatment.

Conclusions

LINAC radiosurgery was highly effective for the treatment of parasagittal meningiomas in this series. For small to medium sized meningiomas with clear invasion of the sinusal lumen, radiosurgery is a reasonable option as a first line treatment. Either alone or combined to conventional surgery, radiosurgery may improve control rate for parasagittal meningiomas.

242 – Poster presentation

Does the Real-Time Thermal Damage Estimate Allow for Estimation of Tumor Control after MRI-guided Laser Ablation? Initial Experience with Recurrent Intracranial Ependymomas

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Introduction
Although control of intracranial ependymomas is highly correlated to degree of surgical resection, it is unknown if the same is true for MRgLITT. We report our experience with MRgLITT for ependymoma and examine the utility of the real-time thermal damage estimate (TDE), a recent software advance, for ablation completion and impact on tumor control. To our knowledge, this is the largest single-center experience with MRgLITT for ependymoma.
Methods
Five tumors in four patients were treated with the Visualase Thermal Therapy System. Two tumors were treated similarly on recurrence. Ablation was performed using a 980 nm diode laser with a real-time image acquisition system (Visualase, Inc). Single-plane TDEs were calculated and compared to original lesion area to compute percent area ablated (PAA). Volumetrics were analyzed; percent volume ablated (PVA) was estimated and correlated with the TDE. Tumor control was correlated with the TDE and volumetric data during treatment.
Results
Nine ablations were performed on five tumors; two had multiple recurrences. Average pre-treatment lesion volume was 8.4±6.3 cm^3; average largest two-dimensional area was 5.4±2.7 cm^2. Averaged TDE was 4.0±2.1 cm^2; average percent area ablated (PAA) was 73±34.3%. Average percent volume ablated (PVA) was 64±23.5%. For subtotal ablations, average recurrence time was 4.4±5.7 months; one adult case remains recurrence-free at 40 months. Using TDEs, correlation analysis of recurrence-time to PAA had an $r = 0.93$ ($p=0.01$), and to PVA showed a correlation with $r = 0.88$ ($p=0.02$). Furthermore, PVA and PAA were correlated with $r = 0.88$ ($p=0.02$).
Conclusions
Through the PAA, the real-time TDE correlated with the volume of ablation in this initial investigation. Furthermore, the TDE and volumetric data corresponded to the level of tumor control, with time to recurrence dependent on ablation completeness. MRgLITT may have a role in the management of recurrent ependymomas, especially with recent software advances.

243 – Poster presentation

Validation of CT-MRI Fusion for Intraoperative Assessment of Stereotactic Accuracy in DBS Surgery

Zaman Mirzadeh, Kristina Chapple, Meg Lambert, Rohit Dhall, Francisco A. Ponce
Phoenix, AZ

Introduction
DBS is typically performed with intraoperative microelectrode recording (MER) and test stimulation for target confirmation. Recent studies have shown accurate and clinically efficacious results following lead placement without MER or test stimulation, using interventional MRI (iMRI) or intraoperative CT (iCT) for verification of accuracy. The latter relies on CT-MRI fusion software. To validate CT-MRI fusion in this setting, we compared stereotactic coordinates determined intraoperatively using CT-MRI fusion to those obtained on postoperative MRI (postMRI).
Methods
DBS electrodes were implanted with patients under general anesthesia. Direct targeting was performed on preoperative MR images, which were subsequently merged with pre-implantation iCT images for stereotactic registration and post-implantation iCT images for accuracy confirmation. MRI was obtained 6 weeks after surgery for comparison.
Results
Postoperative MRI was obtained for 48 patients that had 94 DBS leads placed over a 1-year period. Vector error of the targeted contact relative to the initial plan was 1.1±0.7 mm on iCT and 1.6±0.7 mm on postMRI. Variance comparisons (F-tests) revealed the discrepancy between iCT- and postMRI-determined errors was attributable to measurement error on postMRI, as detected in inter-rater reliability testing. In multivariate analysis, improved lead placement accuracy was associated with frame-based stereotaxy with head of bed at 0° compared with frameless stereotaxy with head of bed at 30° ($p=0.037$).
Conclusions
Intraoperative CT can be used to determine accuracy of lead placement in DBS surgery. The discrepancy between coordinates determined intraoperatively by CT-MRI fusion and postoperatively by MRI can be accounted for by inherent measurement error.

244 – Poster presentation

3D Position of STN in T2 weighed MR Images Compared to Stereotactic Atlasesfor Functional Neurosurgery Planning

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Introduction
Currently there are several standard atlases available that are used to localize the STN in functional MRI studies and clinical procedures such as deep brain stimulation (DBS). However, current atlases are based on low sample sizes and restricted age ranges (Schaltenbrand and Wahren; Morel), and hence the use of these atlases effectively ignores substantially individual differences in brain structural and the changes associated with aging. Here we aimed to compare the position and the volumen of STN observed in the T2 weighted MR images in comparison the same structure in the Schaltenbrand and Morel atlases.
Methods
10 Parkinson patients who underwent STN DBS, received anatomical 3D reconstruction of MRI T2 modified sequence fused with stereotomography, atlas integration, volumetric and spatial comparison of the STN related to the AC-PC using the Schaltenbrand / Wahren and Morel atlases.
Results
We found an important anatomical variation related with patient age, which induces an error on the atlas interpretation, the mean variation in the caudal part of the STN was 2.5 mm. We also found a convergence zone common to all used atlases with an important relevance for future DBS implant studies. STN was always medial to proposed STN by the Schaltenbrand atlas and lateral to STN in Morel atlas.
Conclusions
Our series found Morel atlas to be more accurate in relation to patient image T2 modified series than Schaltenbrand in which we found a lateral posterior deviation. The comparison between patients concludes that no target should be based only on atlas anatomy but the sum of MER, an anatomical atlas and atlas based coordinates from the MCP. We may also advise to mostly rely on the MRI image.

245 – Poster presentation

The Utility of Skull Pin Registration for Frameless Stereotactic Laser Trajectory Planning in Magnetic Resonance Guided Thermal Therapy

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New Brunswick, NJ

Introduction
Magnetic Resonance Guided Laser Induced Thermal Therapy (MRgLITT) has been used to treat conventionally inoperable tumors; however, successful MRgLITT procedures require accurate stereotactic registration and optimal laser catheter placement within the target. We report the use of skull pins, compare it to other registration methods, and determine the ideal number for accurate registration.
Methods
Study data was derived from three years of MRgLITT and included tracer, scalp fiducial and skull pin registration. Data collected included: target alignment errors, registration errors, and laser catheter placements. Laser catheter placement was classified as optimal or suboptimal (greater than 2mm from target). Comparisons of registration error and trajectory length were made using Student's t-test. Standard errors were used to determine ideal number of skull pins necessary to achieve sub-millimeter registration accuracy.
Results
One hundred three laser catheter placements in 8 tracer, 26 scalp fiducial and 49 skull pin registration cases were chosen for this study. Laser catheter placement was suboptimal in 33% of tracer (n=12), 14% of scalp fiducial (n=29) and 6% of skull pin cases (n=62). Both trajectory length ($p=0.075$) and target alignment error ($p=0.21$) showed no correlation with optimal laser catheter placement. Registration errors using scalp fiducials and skull pins were 2.19 ± 1.21mm and 0.46 ± 0.19mm, respectively ($p<0.0001$). Average trajectory length and target alignment errors between tracer, fiducial and skull pin registration cases were not significantly different. Analysis of registration errors based on number of skull pins revealed significant differences between four and five pins ($p=0.00019$), but no significant decreases as additional skull pins were registered.
Conclusions
Skull pins can be used for MRgLITT planning and are associated with increased registration accuracy and optimal laser placement. In order to achieve a 94% accuracy rate in laser placement using frameless stereotaxy registration, the registration error must be less than 1.0 mm. The minimum number of skull pins to achieve this is 5.

246 – Poster presentation

Characterizing the Role of the Hyperdirect Pathway in Subthalamic Deep Brain Stimulation using 7T MRI Data

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Cleveland, OH, and Minneapolis, MN

Introduction
Subthalamic nucleus (STN) deep brain stimulation (DBS) is an established therapy for advanced Parkinson's disease. However, the underlying mechanisms of action and specific brain pathways directly modulated by the stimulation are not well understood. Multiple lines of evidence have recently shown that the hyperdirect pathway (layer V projections that send a collateral to STN) is activated by subthalamic DBS and implicated its role in the therapeutic mechanisms.
Methods
Tractography results derived from diffusion-weighted imaging can enable definition of the trajectories of white matter pathways within the brain on a patient-specific basis. However, typical clinical image quality for such analysis suffers from low signal-to-noise ratio and large voxels. Therefore, we employed cutting edge pre-operative 7T imaging paradigms in Parkinson's disease patients prior to their DBS surgery. We then developed a novel methodology that combines DBS modeling with tractography to explicitly quantify the spatial extent of axonal activation due to the DBS electric field. These tractography-activation models (TAMs) enable comparison of the different activated pathways as the stimulation parameter settings are changed in a patient. This study was specifically focused on characterizing DBS of the hyperdirect pathway. Probabilistic tractography, calculated using FSL, was used to define the pathway in each patient, the voltage distribution for the stimulation settings was calculated using finite element modeling, and the axonal response to the corresponding extracellular voltages was simulated in multi-compartment axonal models with NEURON.
Results
Our patient-specific 7T TAMs predict that direct activation of the hyperdirect pathway is dependent upon the location of the active electrode contact and the stimulation parameter settings. Dorsally positioned contacts preferentially activate the hyperdirect pathway and pathway recruitment increases non-linearly with stimulus amplitude.
Conclusions
Patient-specific TAMs developed with high-field MRI data have potential to enhance our understanding of the specific pathways responsible for therapeutic benefit from DBS.

247 – Poster presentation

Stereotactic Guided Percutaneous Glycerol Rhizotomy for Trigeminal Neuralgia

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Introduction
Medically refractory trigeminal neuralgia and atypical facial pain can be challenging conditions to treat. One of the accepted surgical treatment options is the percutaneous rhizotomy. This procedure is often difficult to master since it is a one-person procedure and requires traversing a number of potential bony obstacles over a long trajectory. Stereotactic guidance could offer an effective and simple technique for efficient cannulation of the foramen ovale for percutaneous glycerol rhizotomy in the treatment of medically refractory trigeminal neuralgia.
Methods
A total of 26 patients with trigeminal neuralgia or atypical facial pain were treated with a stereotactically guided percutaneous rhizotomy. All of these patients had failed an initial attempt at stereotactic radiosurgery and this was a secondary strategy. In each case, general endotracheal anesthesia was induced, the patients were placed in Mayfield pins in a sitting position, and Stealth neuronavigation was utilized to determine a trajectory to the foramen ovale. Stealth guidance views were then used to refine the actual introduction and advancement of the spinal needle. This allowed for efficient cannulation of the foramen ovale and enabled safe and effective percutaneous introduction of glycerol to the ganglion of the trigeminal nerve.
Results
All patients had successful cannulation of the foramen ovale on either the first or second attempt. Residents completed the majority of these cannulations. Long-term follow-up for these patients showed 15 of 26 patients (58%) reporting complete pain control. This was felt to be a good outcome given that all of the patients had previously failed at least one procedure.
Conclusions
Stereotactic guidance as described here compares well with the more commonly published CT-guided trigeminal rhizotomy and the frameless and pinless stereotactic system. This same technique could be utilized for glycerol, radiofrequency or balloon compression rhizotomies.

248 – Poster presentation

Visualase: A New Tool for Biopsy plus Thermal Ablation of Intracranial Lesions

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Introduction

The Visualase Procedure is FDA approved for the treatment of intracranial pathologies including primary and secondary brain malignancies, radiation necrosis and epileptic foci. The system relies on the stereotactic placement of a thin probe to targeted regions within the brain, whereby laser induced thermal therapy (LiTT) is then performed under monitoring with real-time MRI producing thermonecrosis of the lesion.

Methods

After IRB approval, retrospectively charts were reviewed to obtain clinical and radiologic data for patients having undergone treatment with LiTT. Specific data items evaluated include: radiographic findings prior to and after the procedure; demographics; previous medical, surgical or radiotherapies; clinical and functional outcomes obtained at routine follow-up evaluations; patient survival status; and any complications associated with therapy.

Results

Thirty-seven patients have been treated with LiTT since September 2012. Minimal of 2 month follow-up data is available for 33 of these patients. Mean follow-up is 6.64 months (range 2 to16 months). Thirty-three patients had primary or secondary brain tumors, all of which had undergone extensive previous treatment: resection(s), brain radiation (+/- salvage SRS) and chemotherapy. Biopsy showed that 15 had radiation necrosis/ treatment effect, 13 had recurrent tumor, 4 had a mixture of tumor recurrence and treatment effect. Four patients were treated for intractable epilepsy and appropriately had seizure reduction. The procedure was tolerated well by all patients without complication and they were discharged home after an overnight stay. LiTT was found to have a precise lesioning effect, often with longstanding local results, though secondary disease progression occurred in a subset of patients.

Conclusions

LiTT was safe and well tolerated. Visualase is a new tool, allowing biopsy plus thermal ablation. In addition to local disease control, it may reduce the need for repeat craniotomy in clinical decision making regarding re-radiation and chemotherapy.

100: Sunday, June 1, 2014, 11:04-11:14 am; GS #1
Pallidal-Cortical Beta Coherence is Activity-Modulated but not Causally Related in Parkinson's Disease

Mahsa Malekmohammadi, William Speier, Nader Pouratian
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Introduction
Beta band (12-35 Hz) local field potential (LFP) activity is a pathophysiological biomarker of Parkinson's disease (PD) that has been described both in the cortex and basal ganglia that could be used for closed-loop neuromodulation. Using simultaneous cortical-subcortical LFP recordings in patients undergoing deep brain stimulation (DBS) implantation, we define temporal and causal relationships in activity-dependent modulation of beta band activity across cortical-subcortical sites.
Methods
Data was recorded in three patients undergoing pallidal (GPi) DBS implant (off medication), using the DBS electrode for pallidal recordings and an eight-contact electrocorticographic strip placed over the motor cortex. Using 2400 Hz sampling rate, LFPs were recorded while patients alternated between rest and cued, self-paced hand movement. Raw signals were analyzed for activity-dependent changes in power spectral density and cross-site coherence using a multitaper method. Causality was assessed using adapted Granger causality with surrogate analysis to find statistical significance.
Results
Activity-related suppression of beta power was broadly observed across cortical contacts, with the greatest suppression over the motor cortex region. Likewise, activity-related beta suppression was noted in the GPi, largely in ventral contacts. The strongest cross-site coherence was observed between ventral GPi contacts and the ECoG contact with the greatest activity-dependent beta suppression. Activity-dependent cortical-GPi coherence suppression was also observed. While a causal flow of beta activity from GPi to cortex was hypothesized, such a relationship was not identified.
Conclusions
Despite activity-dependent suppression of cortical and subcortical beta power and cross-site coherence, there is no consistent evidence of causal flow of beta activity across these two sites. These findings directly challenge the hypothesis that the basal ganglia impose an "akinetic" beta rhythm in PD patients. Further characterizing the modulation of synchrony between GPi and motor cortex is critical for future investigation to explain the circuitry of PD.

119: Monday, June 2, 2014, 2:20-2:30 pm; PS #3
Real and Imagined Gait Modify Neural Network Dynamics in the Pedunculopontine Nucleus

Timothy Tattersall, Terence J. Coyne, Peter Silburn, Raymond Cook, Paul Silberstien, Francois Windels, Peter Stratton, Pankaj Sah
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Introduction
The pedunculopontine nucleus (PPN) is a part of the mesencephalic locomotor region and thought to play a key role in the initiation and maintenance of gait. In some patients with PD, levodopa provides good control of motor symptoms other than for freezing of gait (FOG) and falling. In these patients these symptoms can be alleviated by deep brain stimulation (DBS) in the PPN. However the role of the PPN gait control is not understood. We recorded neural activity in the PPN to study its role in the control of movement.
Methods
We studied 11 patients with PD who had FOG. During microelectrode recording single unit recordings were obtained under resting conditions, during limb movement, and during imagined gait.
Results
We identified two types of neuron in the PPN – narrow and wide units. Wide neurons had broader spikes, more burst characteristics, and were more prevalent in the caudal PPN, suggesting they are cholinergic neurons. Neurons in the PPN responded to limb movement as well as imagined gait. Neurons in the PPN discharged as networks, and distinct networks were engaged by limb movement and imagined gait. Wide neurons were more prominent in these networks.
Conclusions
These results show that PPN is not only involved control of gait, but plays a role in planning movement. Moreover, activity in the PPN is mediated by networks of neurons that are dynamically mediated during planning of movement. These results suggest freezing of gait may result from disrupted network activity in the caudal PPN. DBS in the PPN may alleviate freezing of gait by modulating network activity in the PPN.

121: Monday, June 2, 2014, 2:40-2:50 pm; PS #3

Long-term Outcome of the Posterolateral Globus Pallidus Internus Deep Brain Stimulation in Patients with Tourette Syndrome

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Introduction
Numerous anatomical targets for deep brain stimulation (DBS) have been proposed for the treatment of patients with severe Tourette syndrome (TS), who are refractory to pharmacological and psychotherapeutic treatment. However, there is no consensus on the most appropriate DBS target site. Several case reports demonstrated clinical benefits of the globus pallidus internus (GPi) DBS in TS patients with< 2-year follow-up. Moreover, a complicating issue of GPi target is the differential anatomic- functional distribution of both motor and limbic circuits throughout the GPi, the limbic region lying anteromedial while the motor region located posterolateral and inferior, with some considerable distance between them.
Methods
We retrospectively assessed the long term clinical outcome of 13 Chinese TS patients who are refractory to pharmacological and psychotherapeutic treatment, and underwent DBS targeting the posterolateral region (motor region) of the GPi. The primary outcome was a change in tic severity as measured by the Yale Global Tic Severity Scale (YGTSS) and the secondary outcome was a change in associated behavioral disorders and mood as measured by Tourette Syndrome–Quality of Life Scale (TSQOL) assessment.
Results
The average reduction in the total YGTSS scores at last follow-up (mean 43 months, range 13-80 months) compared with baseline was 52% (range 4-84%), and the mean improvement rates of the 1 month, 6 months, 12 months, 18 months, 24 months and 36 months to the baseline were 12%, 20%, 27%, 34%, 42%, 47% and 55%, respectively. We noticed significant improvement of tic symptoms after 6 months of DBS programming ($p<0.05$). The TSQOL score has improved by an average of 46% (range 11-77%).
Conclusions
This study provides the largest reported GPi DBS case series of 13 treatment-refractory TS patients with longest follow-up, and supports the potential beneficial effect of posterolateral GPi DBS on disabling tic reduction and improvement of quality of life.

249 – Poster presentation

Clinical outcomes following bilateral GPi "Asleep" DBS for Parkinson's disease

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Introduction
Recent studies show DBS can be performed safely and accurately under general anesthesia without microelectrode recording or test stimulation. The procedure couples techniques for direct anatomical targeting on MRI with intraoperative imaging for verification of stereotactic accuracy. However, few studies have examined the clinical outcomes of these patients.
Methods
This is a prospective study of 20 patients with advanced PD who underwent bilateral GPi electrode placement under general anesthesia. The primary outcome measure was the change in off medication UPDRS III score at 6 months. Secondary outcomes included effects on PDQ-39, UPDRS III on medication, UPDRS IV, and levodopa equivalent dose (LED). DBS lead locations, adverse events, and stimulation parameters were documented.
Results
The mean patient age was 59 years (14M/6F). The mean UPDRS III off medication score improved from 47 to 28 (39.6%) at 6 months ($p<0.001$). Although mean PDQ-39 scores (47.0 vs. 41.4; $p=0.28$) and LED (1182 vs. 1060 mg; $p=0.15$) also improved, these differences were not statistically significant. Average lead location was 20.8 mm lateral, 2.3 mm anterior, and 3.6 mm inferior to the midcommissural point, with mean vector error 1.2±0.9 mm relative to intended target. There were no significant adverse events.
Conclusions
GPi leads placed under general anesthesia using direct anatomical targeting resulted in significantly improved outcomes as measured by the UPDRS III off medication score at 6-months.

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Bilateral Globus Pallidus Internus Deep Brain Stimulation for Dystonic- Choreoathetoid Cerebral Palsy in Children

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Introduction
Children with cerebral palsy (CP) may present with dystonia-choreoathetosis, which is a significantly disabling movement disorder. Here, we investigate the effectiveness of globus pallidus internus (GPI) deep brain stimulation (DBS) in children with dystonic- choreoathetoid CP.
Methods
A retrospective study of four patients with dystonic-choreoathetoid CP was conducted between May 2011 and October 2013. The primary efficacy endpoint was the relative change of the Burke-Fahn-Marsden Dystonia Rating Scale (BFMDRS) after DBS. The DBS leads and internal pulse generator were implanted in one session under general anesthesia and microelectrode recording.
Results
The mean age at DBS implantation was 10.75 years (range 7–14 years). The mean follow-up period was 8.5 months (range 5–11 months). The stimulation parameters are as follows: 130 Hz, 60–90 μs, 2–3.6 V. The BFMDRS movement score was from 52.6 to 38.9 after DBS. The dystonic component and spasm responded to DBS more than the choreoathetoid movements. One patient had a direct trauma to the internal pulse generator that required a replacement.
Conclusions
Bilateral GPI-DBS resulted in functional benefit for pediatric patients with dystonic-choreoathetoid CP. It could be considered a treatment option for this group of patients. The small group of patients limits the findings of this study and mandates further investigation with a large group of patients.

251 – Poster presentation

Offsets Based on Microelectrode Recording in DBS: Moving Towards or Away From Our Initial Plan?

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Introduction
Microelectrode recording (MER) and test stimulation are used intraoperatively to optimize lead placement in DBS surgery. Advances in neuroimaging have provoked consideration of direct structural targeting and stereotactic accuracy as surgical endpoints in DBS, implicitly challenging the utility of MER. We examined whether offsets from initial trajectory directed by MER or test stimulation moved us closer or further from the planned target.
Methods
Over a 2-year period, we identified 35 DBS leads in 29 patients that were positioned through a directional offset intraoperatively based upon information from MER or test stimulation. After final lead placement, these patients had intraoperative CT (iCT) scans fused to preoperative MR planning images to verify targeted contact location. The coordinates of the targeted contact prior to the offset were extrapolated from the final coordinates and the known offset vector.
Results
The mean Euclidean errors between the preoperative plan and the targeted contact coordinates before and after the MER-directed offset were 3.0 and 2.5 mm, respectively ($p=0.015$). In 25 of 35 cases (71.4%), the offset moved the lead closer to the initial plan. We found no association between the likelihood of moving towards the initial plan and the number of additional trajectories (mean 2.4), the electrophysiological indication for the offset (recordings: 37%, motor thresholds: 31%, sensory thresholds: 26%), or the targeted nucleus (GPi: 51%, STN: 17%, VIM: 31%).
Conclusions
The majority of offsets directed us closer to the coordinates of the initial plan, suggesting that the initial surgical plan was appropriate, and MER and test stimulation served to help correct for stereotactic inaccuracy.

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Smartphone Application to Improve Gait in Parkinson's Disease

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Introduction

One of the most debilitating motor symptoms of Parkinson's disease (PD) is gait dysfunction. Despite the benefits of current pharmacological and surgical therapies for patients with PD, treatment effectiveness and options for gait difficulties remain limited. Evidence exists to support the use of rhythmic external auditory signals to improve PD patients' gait. We analysed the effects on gait of an original smartphone app that generates auditory rhythmic cues matching step frequency to the auditory rhythm aiming to improve walking in PD patients.

Methods

The application – Listenmee® (Brainmee, Madrid-Spain [www.brainmee.com]) was developed on a mathematical basis allowing users to choose an intra-individually auditory cueing rate (beats/min). The employed technology is simple and easy to use. Users can access it through a direct touch screen ordering system with commands such as "PLAY", "PAUSE" and a circle type interface on the screen. The user is able to use the mobile touch screen to increase (clockwise) or decrease (against clockwise) the cueing rate. The application has different cueing rates as follows: very slow [0% -50%], slow [51% -100%], fast [101% -150%] or very fast [151% -200%]. The applied frequencies can vary between 60 to 480 Hz. Patient and physician together can choose the sound set and cueing rate that is best suited for the patient.A volunteer sample of 10 PD patients between 45 to 65 years old (3 women and 7 men) (5 with previously implanted STN DBS) were studied, all with gait disturbances. Auditory rhythmic cues were administered through the device - Listenmee® app in a single session.

Results

ait performance in this study achieved an important mean improvement in the three major dependent variables: in walking speed (meters per second) of 63.38%, cadence (steps/min) 22.11% and stride length in meters 109.19% in a singular session analyses.

Conclusions

Listenmee® is a safe and effective adjunct help for symptomatic improvement of gait in patients with PD including freezing of gait. Clinical application of auditory cues may be another model in the armamentarium of therapies for treatment of patients with PD. Further analysis also should involve chronic responses to the cues in PD patients and in other diseases.

253 – Poster presentation

Combined Thalamic and Pallidal Deep Brain Stimulation in Patients with Secondary Hemidystonia: Two Targets are Better than One

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Introduction

Secondary dystonia is often poorly responsive to medications. The optimal target for the treatment of secondary dystonia with deep brain stimulation (DBS) is not established. A number of thalamic nuclei as well as the globus pallidus and the subthalamus have been tried. With the rationale that two targets may be better than one, we implanted patients with secondary dystonia with both thalamic and pallidal DBS electrodes.

Methods

We reviewed 9 consecutive patients with secondary hemidystonia who underwent both thalamic and pallidal DBS either simultaneously or staged between 1997 and 2014. We tested the efficacy and safety of stimulating at either one or two targets or both targets simultaneously.

Results

In this series, the most common etiology of dystonia was stroke (4 patients), followed by perinatal injury (2 patients). Eight patients had a simultaneous thalamic and pallidal stimulation. One patient had a thalamic stimulation as a salvage procedure after loss of benefit of pallidal stimulation. At the last follow up; five patients showed increased benefit with activation of both pallidal and thalamic electrodes compared to with stimulation at a single target. In one of these patients thalamic DBS improved proximal leg dystonia, while stimulation of the ventral contacts in the GPi improved distal dystonia and dorsal contacts improved proximal dystonia. None of the above patients experienced any surgical related complications, except for the patient who had a staged procedure. A fractured pallidal electrode was discovered intra-operatively at the time of thalamic electrode insertion.

Conclusions

Simultaneous unilateral thalamic and pallidal deep brain stimulation is a reasonable and safe therapeutic option, which could increase the beneficial effect of deep brain stimulation and expand the programming options in the challenging cases of secondary hemidystonia.

254 – Poster presentation

Quality of Life in Advanced Parkinson's Disease after Bilateral Subthalamic Stimulation: 2-Year Follow-up Study

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Introduction

The aims of this study were to assess quality of life (QoL) using Parkinson's Disease Questionnaire PDQ-39 after bilateral subthalamic nucleus (STN) deep brain stimulation (DBS) and to find any correlations between changes in UPDRS scores and separate PDQ 39 QoL dimensions and PDQ summary index (SI) score at long-term follow-up.

Methods

We evaluated 16 patients with advanced PD after bilateral STN DBS. All 16 patients were assessed 1 year after surgery and 14 were studied 2 years after surgery. Patients were assessed using Unified Parkinson's Disease Rating Scale (UPDRS) in medication on and medication off conditions preoperatively and postoperatively. All UPDRS evaluations were performed postoperatively during stimulation on condition. The QoL was evaluated by applying PDQ-39 questionnaire.

Results

The UPDRS scores after 1 and 2 years in medication off and on condition when bilateral STN DBS was switched on have shown significant difference between baseline scores and follow up scores (both in off and on conditions) in every measurement of UPDRS except mentation after 2 years. All dimensions of PDQ-39 as well PDQ-39 SI score were highly significantly improved after 1 year. The same improvements were visible in 2 years follow up except for social support and communication. We have found a positive correlation between ADL UPDRS, motor off UPDRS scores, dyskinesia UPDRS score and PDQ-39 mobility, ADL and PDQ-39 SI score. We have observed a negative correlation between improved fluctuation UPDRS score and PDQ-39 mobility. We have found no correlation between the duration of off period and daily medication equivalency units and changes in PDQ-39.

Conclusions

STN DBS significantly improved all dimensions of PDQ-39 at 2 years follow-up except for social support and communication. We have observed positive correlations between improvements in UPDRS scores and several PDQ-39 dimensions and PDQ-39 SI score at 2 years follow-up.

255 – Poster presentation

Differences in Dopamine Transporter Imaging in Patients with Parkinson's Disease Treated with Subthalamic Deep Brain Stimulation and Contralateral Thalamotomy

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Introduction

Single-photon emission computed tomography (SPECT) with ^{123}I FP-CIT is a marker for loss of presynaptic dopamine transporters in the striatum in Parkinson's disease (PD). The mechanisms by which deep brain stimulation (DBS) of the subthalamic nucleus (STN) leads to clinical benefit in PD, especially with regard to dopaminergic transmission, remain unclear. Therefore, the objective of our study was to evaluate alterations of synaptic dopaminergic signaling in patients treated with unilateral STN-DBS and contralateral thalamotomy

Methods

We used ^{123}I FP-CIT SPECT in order to evaluate binding to the dopamine transporter in Parkinson`s disease in 3 patients submitted to unilateral STN DBS and contralateral thalamotomy. They were examined with ^{123}I FP-CIT SPECT pre-operatively, and 6 and 12 months after surgery.

Results

Pre-operatively, all patients already had substantial signs of severe nigrostriatal neuronal loss as determined from the ^{123}I FP-CIT SPECT scans. One year after surgery the specific ^{123}I FP-CIT binding to the striatum was significantly more reduced on the thalamotomy side than on the DBS side ($p< 0.05$), when compared with the preoperative baseline scan.

Conclusions

The specific binding of ^{123}I FP-CIT was more reduced on the lesion side than in the stimulated STN DBS side. Our study suggests that STN DBS could exert a neuroprotective effect compared to the lesion. More patients and follow-up are necessary

256 – Poster presentation

A Stochastic Dynamical Model Signifies the Potential Effectiveness of Temporally Non-Regular Subthalamic Nucleus Deep Brain Stimulation

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Introduction
Recent evidence points to the potential importance of the temporal pattern of high frequency deep brain stimulation (DBS) in the clinical efficacy of this reference neurosurgical procedure. At the same time, alterations in the abnormal discharge pattern of subthalamic nucleus (STN) neurons and disruption of neuronal synchronization have been suggested to be involved in the therapeutic mechanisms of action of STN-DBS. In this study, we employ methods from stochastic nonlinear dynamics to comparatively simulate the desynchronizing effect of regular versus non-regular stimulation patterns, based upon microelectrode recordings (MERs) acquired during 10 surgical interventions, in patients with Parkinson's disease (PD).
Methods
A stochastic phase model is fitted to a total of 63 MERs corresponding to sites lying within the intraoperatively confirmed borders of the STN. The phase model is developed encompassing multiple factors affecting neuronal dynamics, i.e. neuronal coupling, intrinsic independent and extrinsic common noise sources, and the absence/presence of external forcing. Through this model, we comparatively evaluate the Lyapunov exponent as a quantity reflecting subthalamic synchronization dynamics in response to periodic (130 Hz) versus non-regular inputs. Non-regular inputs are generated by a gamma process with the same mean frequency (130 Hz) and different degrees of temporal variability. Positive values of the Lyapunov exponent indicate desynchronization.
Results
The desynchronizing effect of both stimulation patterns compared to baseline (off stimulation) is captured and validated by the proposed model ($p<0.05$). Most importantly, with increasing temporal variability, non-regular inputs yield a significantly greater Lyapunov exponent compared with regular stimulation, at the 5% significance level.
Conclusions
The presented modeling approach provides further corroborating evidence regarding the prominent role of non-regular stimulation patterns in the therapeutic outcome of DBS in patients with PD. For future work, extensions of the model will be considered in order to elucidate the role of specific characteristics of temporally irregular stimulation patterns.

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The Use of Surface Electrography as a Troubleshooting Tool in Deep Brain Stimulation

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Introduction
Hardware failures related to both pulse generators and leads can be a challenge in patients with deep brain stimulation. The available onboard tools of the implantable pulse generators (IPG) are often unsatisfactory, making an efficient troubleshooting difficult. Moreover they may deliver ambiguous information. Especially in therapy failures this can be a problem, because it remains open whether the reason for this failure is either medical or hardware related. False positive alerts may lead to unnecessary surgical steps like replacement of the leads or the extensions.
Methods
The principle of surface electrography is that every single pulse emitted by an implanted pulse generator can be recorded using standard skin electrodes, amplified and displayed by a medical oscilloscope. The voltage drop is proportional to the tissue impedance. The latter is a constant for an individual body. Differences in voltage drop or missing spikes are highly suspicious for contact problems respectively lead fractures. According to the used stimulation technology, constant current or constant voltage, the stimulation pulse shapes are either rectangular or more complex. Every single pole is analysed individually. We are using an iOS based (iPad Apple) oscilloscope for performing these tests.
Results
The present procedure was performed in a total of 60 patients with DBS systems where routine measurements of the impedance using the standard procedure (self test of the IPG) had either given ambiguous results or values suggesting a fracture of the lead extension. Only in six of these patients surface electrography corroborated these findings and consecutive replacement of the lead extension finally confirmed the presumed fracture. In another five patients the sudden loss of therapy was related to the IPG resulting in a change of the pulse curve. In all eleven patients efficient therapy resumed after surgical revision and they returned to normal surface electrography. We did not observe false positive results.
Conclusions
Surface electrography a safe and easy diagnostic and troubleshooting procedure in cases where hardware failures are suspected to be the reason for a loss of DBS therapy.

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Simultaneous Bilateral MER-Guided Stereotactic Implantation of Deep Brain Stimulation Electrodes

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Introduction
Bilateral DBS has become one of the most important neurosurgical techniques for the treatment of many neuropsychiatric diseases. In recent years, many efforts have been made in order to improve safety, accuracy and comfort for the patient treated by DBS. A cardinal fact is that currently the surgical step-by-step procedure involves two unilateral sequential hemispherical implants what increases surgical time and also CSF leak increasing the risk of brain shifting. In this case series we performed bilateral, simultaneous implant of deep brain electrodes, as a strategy to shorten surgical procedure avoiding major brain shift. The aim of this work was to demonstrate technique feasibility and advantages of performing bilateral simultaneous electrodes implant in the subthalamic nucleus (STN) from a case series of 10 patients with Parkinson´s disease (PD) and 1 with primary dystonia
Methods
Two half-arcs were mounted simultaneous on a Micromar® stereotactic frame allowing simultaneous bilateral access. After two simultaneous precoronal approaches, one to five cannulas were introduced through two microdrives until 10 mm before target, microrecording was performed simultaneously at every 0.5-mm until target. The number of tracks used for macroelectrode insertion ranged from 1 to 3 (median 1) and the macroelectrode in track eliciting the best clinical outcome was subsequently replaced by a permanent electrode (Medtronic® type 3389). Immediately after the procedure, the position of each permanent electrode was verified by orthogonal X-ray images.
Results
No dislocation higher than 1-mm was found in any patient. The procedure presented major advantages over traditional unilateral individual consecutive approach, such as: real time recorded bilateral neuronal activity, high accuracy between planning and surgery documented by better clinical outcomes most probably due to avoiding of major brain shifting, and over 1 hour shorter total operating time with a total intracranial surgical time of 116.3 ± 22 min.
Conclusions
Bilateral simultaneous implant of deep brain electrodes had the advantage of considerable time saved, simultaneous micro electrode recording and minor brain shifting making DBS surgery more accurately.

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Spatial Topographies of Unilateral STN DBS Efficacy for Ipsilateral, Contralateral, Midline and Total Parkinson Disease Motor Symptoms

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Introduction
STN DBS has become a successful intervention for medically refractory Parkinson Disease, although its efficacy depends on optimal surgical placement of the active electrode. While the predominant clinical effect is observed contralaterally (CL), modest improvements in ipsilateral (IL) and midline symptoms (ML) are also observed to contribute to the overall therapeutic effect. This study elucidates the role of active contact location of unilateral DBS on the contralateral, ipsilateral and axial subscores of Parkinson's Disease motor symptoms.
Methods
In 2005-2009, 86 consecutive patients receiving first DBS STN electrode placements were identified, yielding 73 patients with comprehensive 3 month follow-up. The total pre-operative and post-operative UPDRS Part III scores were rigorously obtained, and divided into CL, IL, and ML subscores. Active contact locations were defined as the cathode contact, whose location was determined upon the immediate post-operative MRI scan, normalized to the length of the AC-PC line. 3-D ordinary "kriging" algorithm was employed to generate spatial interpolations for the total, IL, CL, and ML symptom categories (measured in % reduction). Interpolative reconstructions were performed in the axial planes (z=-0.5, -1.0, -1.5, -3.5, -4.5, -6.0), and in the mid-sagittal plane. Interpolation error and significance was quantified using a cross-validation technique and quantile-quantile (q-q) analysis.
Results
There was an overall reduction in UPDRS Part III symptoms: Total = 37.0%±24.11% ($P<.05$), IL= 15.9%±51.8%, CL=56.2%±26.8% ($P<.05$), ML= 26.5±34.7%. Kriging interpolation was successfully performed and cross-validated with q-q analysis with high correlation ($R2 >.92$), and demonstrated regions of efficacy (ROE) for each symptom category. While contralateral symptoms demonstrated broad ROE across the peri-STN area, ipsilateral and contralateral ROEs were more restricted and located along the dorsal aspect of the STN and the caudal ZI.
Conclusions
Spatial topographies of STN DBS motor symptom reduction vary for contralateral, ipsilateral and midline symptoms. There exists a unique window at which contralateral, ipsilateral, and midline structures may achieve best efficacy. Surgical optimization should target the intersection of optimal regions for these symptom categories.

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A Centroid-Based Targeting Approach to Facilitate DBS Electrode Placement in the Gpi Using Interventional MRI Guided Surgery

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Introduction
The traditional method for deep brain stimulation surgery in globus pallidus internus (GPi) involves consensus-based direct or indirect targeting, refined by microelectrode recording, mapping, and clinical testing. For interventional MRI (iMRI) - guided DBS placement these essential refinements for effective placement are not available, placing the onus upon direct targeting. However, there remains variability in direct visualization of DBS targets. We present a novel technique to facilitate direct targeting for iMRI-guided DBS surgeries in GPi using patient-specific deformable models and a model centroid-based targeting concept.
Methods
We have developed deformable 3D surface models of basal ganglia nuclei based on a human brain atlas. For each patient the models are interactively modified by affine deformation to best fit individual MRI-visible nuclei and boundaries. The centroid is calculated as the mean of all points of the posterior half of the GPi model surface mesh. The centroid coordinates in 3D Talairach space are used as the target. The DBS lead is placed along the trajectory defined by the brain entry point and the centroid so that its tip reaches the ventral border of the GPi model.
Results
We implanted 39 electrodes in 27 patients, 15 of them had Parkinson's disease (PD) and 8 – dystonia. The mean distance of the clinically effective electrode contact from the centroid was 1.96 ± 1.33 mm. The mean clinical measures at 6 months improved by 38.8±18.3 % in PD (UPDRS) and 65.2±17.7 % in dystonia (BFMDRS).
Conclusions
This novel centroid-based technique facilitated the capture of a suitable target in GPI during iMRI-guided DBS surgery. Using this technique the DBS leads were implanted in a clinically effective location in the absence of microelectrode mapping and clinical testing.

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Postoperative Deep Brain Stimulation (DBS) Impedance Variability in Parkinson's Disease (PD) Patients Implanted with the Boston Scientific Vercise System

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Introduction
Most Deep Brain Stimulation (DBS) systems deliver stimulation using voltage-controlled systems where the delivered current is dependent on impedances. Modeling shows that an impedance change of 450 ohm resulted in a 50% reduction in the volume of tissue activated. It was proposed that instability in impedances could be partialresponsible for the frequent need to reprogram stimulators in DBS patients postoperatively. A current-controlled Deep Brain Stimulation system is expected to better control stimulation in the face of changing impedances. However, data on long-term impedance variability in human DBS patients is limited, and within-patient impedance variability has been proposed to be minimal. In this report, impedance variability in 40 subjects with bilateral DBS over a 52 week period is presented.
Methods
40 patients with idiopathic Parkinson's disease (PD) were implanted bilaterally with Boston Scientific's current-controlled VerciseTM DBS system in the subthalamic nucleus (STN). Subjects' devices were activated 2 – 18 days after implant. The impedances were measured during office visits at activation, 12, 21, 26, and 52 weeks post-implant.
Results
An overall trend of large changes in impedances was observed in these subjects over the entire period evaluated. A high degree of inter-patient variability was observed, with impedances ranging from 574-1512 ohms at activation (n=33, mean=844.8±233, median=778), 919-1583 ohms at 12 weeks (n=28, mean=1182±157, median=1152), 907-1626 ohms at 21 weeks (n=18, mean=1178±186, median=1168), 809-1488 ohms at 26 weeks (n=26, mean=1164±156, median=1158), and 746-1488 ohms at 52 weeks (n=20, mean=1215±202, median=1261).
Conclusions
Impedances in DBS patients vary between and within each patient. This variability over time is similar to that previously reported in animal data. The variability might account for fluctuating effects in voltage controlled DBS systems.

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Subthalamic Beta Activity and Optimal Deep Brain Stimulation Sites Are Spatially Dependent

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Introduction

Deep brain stimulation (DBS) of the subthalamic nucleus (STN) is an effective therapy for Parkinson's disease (PD). However, optimal stimulation sites in the STN region are frequently contested. The aim of this study was to corroborate results from conflicting studies by providing evidence that the relationship between sites of beta hypersychrony and optimal stimulation are spatially dependent relative to the STN region.

Methods

We measured local field potential (LFP) activity in the beta band from 26 subthalamic regions in 13 patients undergoing DBS treatment for PD. We recorded beta LFP data from microelectrodes between 2 mm above the electrophysiological STN to the ventral border and assessed the peak power in the beta band from each recording. 3-T magnetic resonance imaging (MRI) was used to identify the midpoint of the STN. We used postoperative MRI to locate each trajectory relative to the midpoint and the location of the independently chosen contact for chronic stimulation.

Results

Trajectories categorized as medial to the STN midpoint had locations of peak beta power correlated with optimal sites of stimulation. Conversely, trajectories categorized as lateral had locations of peak beta power significantly below optimal contact sites. The optimal contact sites correlated with the dorsal border of the STN in both medial and lateral trajectories.

Conclusion

These results suggest that there is a dependence on location within the STN when using areas of peak beta activity to determine sites of optimal stimulation for DBS in PD patients. These results may have further implications in studies modeling STN beta oscillations, post-operative stimulation parameter selections, and closed-loop stimulation technologies.

263 – Poster presentation

Intrathecal Baclofen for Spasticity: A Compliance Based Study to Indicate Effectiveness

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Introduction

Intrathecal administration of baclofen via a continuous programmable buttery based pump is a recognized option in the treatment of medically refractory spasticity. Objective outcome evaluation is usually based on clinical evaluation of the spastic muscles groups. Such evaluations my not indicate functional improvement in this heterogeneous group of patients. In this study, patient's compliance after two years of implanting the pump device was set as an indication of effectiveness of the treatment as appreciated by the patients themselves or their caregivers.

Methods

A cohort group of 35 patients were admitted to the hospital for an intrathecal baclofen trial. A total of 27 patients were implanted with battery based programmable baclofen pump. All patients were referred to a specialized outpatient clinic for medication refilling and adjustment of rate of infusion. All follow-up visits were supported by national health services and free of any charges including transportation. All patients had either minimum of two years follow-up or discontinuation of therapy for different reasons. All patients' medical data were collected prospectively and reviewed at the time of the study.

Results

Twenty seven patients (15 males and 12 females) were included in the study. Patient`s age ranged from 7 to 69 years (mean of 29 year). Documented etiologies of spasticity included trauma, cerebral palsy, familial spasticity, multiple sclerosis, tumors and others. All patients were operated by the same surgeon (senior author) following the same operative and post operative protocol. At the 2 years post implantation set point, 20 patients continue to comply with the treatment. All of them reported at least moderate improvement in the symptoms that deserve compliance with the therapy. The other 7 patients had the pump removed as decided by the patients themselves or the caregivers (5 patients), recurrent infection (1patient) and death secondary to the primary disease (1 patient).

Conclusions

At 2 years follow-up after implantation of programmable intrathecal baclofen pump therapy for intractable spasticity, 74% of patients continue to comply with the treatment.

264 – Poster presentation

Vercise DBS System in the Treatment of Complex Tremor

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Introduction

The results of conventional treatment for complex tremor (MS related, rubral, dystonic etc) either by surgery or DBS has been historically difficult. In this prospective study we report our early experience with DBS (VIM, Zi/pSTN) in patients with complex tremor implanted with a Boston Scientific 8 contacts DBS lead.

Methods

Ten patients with complex tremor were implanted between 2012-2013. All patients were implanted with NexFrame-Medtronic frameless system, pre operative targeting was a combination of anatomical, atlas based and neurophysiological targeting (MER). DTI tractography was obtained in all patients (definition of VIM in relation of rubro-dento-thalamic tract and cortico-spinal tract). Post-operative lead location was confirmed with CT/MRI fusion with acquisitions of coordinates. Tremor rating scale and QOL were evaluated post-operatively, follow up period was 3-12 months.

Results

All patients showed a significant improvement of their pre-operative tremor. Complete suppression of the tremor was achieved in dystonic and rural tremor. In patients with MS related tremor we achieved good control of all the component of the tremor including the proximal ataxic tremor. We did not experience any intra-operative or post-operative complications. Post-operative CT/MRI fusion showed a satisfactory lead position with negligible vector error. Intra-operative stimulation with current steering was a very user friendly platform an able to define clinical effect and stimulation side effects. DTI tractography was useful in the targeting of VIM (anatomical definition)

Conclusions

The new Vercise DBS system is a very good hardware platform.The novel 8 contacts lead offer a significant flexibility for both targeting and programming. We found this particularly useful in complex tremor when multiple site targeting can be considered. Our early result in patients with complex tremor are encouraging. Larger study and the integration of DTI tractography in the targeting process will be required to confirm the role of an 8 contacts lead in DBS (VIM, Zi/pSTN) for complex tremor.

265 – Poster presentation

Deep Brain Stimulation Troubleshooting: Revision vs. Reprogramming

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Introduction

Deep brain stimulation (DBS) re-programming strategies may spare patients from electrode revision procedures. There are no clear evidence based guidelines regarding appropriate referrals for electrode revision.

Methods

MRIs ordered on DBS patients were identified from database review. Retrospective chart review was performed to identify reason for MRI, clinical features associated with programming, and the outcome of reprogramming strategies or revision. MRIs were analyzed quantitatively to identify electrode location.

Results

Of 42 MRIs ordered, 28 were to identify electrode location. Reasons included: insufficient benefit and side effects (n=13), side effects (n=9), insufficient benefit (n=4), no benefit (n=2). DBS targets included: 15 bilateral subthalamic nucleus (STN), 7 bilateral ventral intermediate (ViM) nucleus of the thalamus, 3 bilateral globus pallidus interna (GPi), 3 unilateral. 25 patients underwent reprogramming (n = 17 before MRI vs n= 8 after MRI). Reprogramming strategies included changing contacts, changing polarity, interleaving, constant current and using groups. Six patients underwent revision of 10 electrodes (3 STN, 2 GPi, 5 ViM). 9 were suboptimally placed (defined as >2mm from intended target). Outcomes of revision were good in 2 patients and insufficient or no benefit with side effects in 4. Of 22 patients managed clinically, 15 (68%) had suboptimal electrode placement. Reprogramming yielded: good outcome without side effects (40%), good outcome with side effects (13%), insufficient benefit with no side effects (27%), insufficient benefit with side effects (7%).

Conclusions

In this study, 33% of patients with side effects or insufficient benefit from DBS re-programming not referred for surgery may have benefited from revision of suboptimally placed electrode(s). Revision only improved outcomes in 30% of referred patients, suggesting that careful assessment of stimulation effects in relation to measured electrode position along with other clinical factors should be considered to improve DBS outcomes.

266 – Poster presentation

Micromapping of the STN and ZI: Noncontiguous Areas of Efficacy

Deepak Kumbhare, Tony Anene Maidoh, Craig R. Kelman, Kathryn L. Holloway
Richmond, VA

Introduction

Efforts to identify the optimal lead location within the subthalamic region have been limited by biased sampling of the region, lack of co-registration of efficacy with MER signature, and the lack of adequate normalization paradigms.

Methods

Intraoperative data was collected on 40 patients undergoing DBS placement in the subthalamic nucleus for Parkinson's disease. Efficacy of stimulation was assessed at 2 mm intervals along every microelectrode track recorded for a total of 493 data points. The data was normalized to a uniform MRI atlas using the adaptive bases algorithm (ABA) for non-rigid registration. The data was segregated based on the MER signature and analyzed separately to determine regions of improved UPDRS scores as well as regions of worsened scores within three dimensional space.

Results

We found statistically significant geographic separation of efficacy from non efficacious regions in both the STN and ZI. These regions were not contiguous. Although bradykinesia and rigidity changes co-localized, tremor efficacy was distinct from these regions.

Conclusions

The fine resolution of our data set and the normalization process has allowed us to discriminate subregions within the STN and ZI with improved efficacy immediately adjacent to areas of worsening efficacy. It is likely that this close approximation has complicated prior efforts to predict outcome using lead location.

267 – Poster presentation

Evaluation of Thalamotomy with DTI Tractography

Shinichi Goto, Terence J. Coyne, Peter Silburn
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Introduction

Stereotactically guided radiofrequency (RF) lesioning of the nucleus ventralis intermedius (Vim) of the thalamus can be effective in relieving intractable tremor. Three patients who underwent stereotactic RF Vim thalamotomy were assessed by (a) reduction in tremor (b) lesion size and (c) fiber connectivity as visualized on diffusion tensor imaging (DTI) tractography.

Methods

Two patients with essential tremor and one patient with Parkinsonian tremor undergoing unilateral Vim thalamotomy participated in this study. The surgical procedure was performed using a Cosman-Roberts-Wells stereotactic frame system. After merging 3-tesla MR data onto stereotactic CT images with a Medtronic Stealth Station, direct Vim targeting was performed. After test stimulation, RF lesions were created using a Baylis Medical PMG-230 lesion generator. MRI with DTI tractography was performed post-operatively to evaluate lesion size and fibre connectivity.

Results

The 3 patients experienced complete tremor suppression contralateral to the lesioned side after surgery, without neurological deficit. There was no change in limb tremor ipsilateral to the lesion. The thalamic Vim RF lesions were smoothly shaped and clearly defined on post-operative MR imaging. Probabilistic fibre tractography demonstrated intact connectivity between the Vim thalamus and the primary motor cortex, premotor cortex, and supplementary motor area, but reduced connectivity (relative to the non-lesioned side) from the Vim thalamus to the cerebellum, including via dentatorubrothalamic tract fibres.

Conclusions

The surgical technique of RF Vim thalamotomy for tremor, utilizing direct stereotactic targeting, was safe and reliable. Our results suggest a satisfactory good clinical outcome may be associated with reduced connectivity of the lesioned thalamic Vim nucleus with the cerebellum as seen on DTI tractography.

268 – Poster presentation

Transcranial Direct Current Stimulation for Gait Disorders in Advanced Parkinson Disease – Pilot Study

Eduardo Urbano da Silva, Nilton Alves Lara Jr, Victor Rosseto Barboza, José Carlos E. Veiga, Rafael Carlos da Silva
São Paulo, Brazil

Introduction
Transcranial Direct Current Stimulation (TDCS) is a promising method of non-invasive brain stimulation to modulate cortical activity. It has been studied in many areas to enhance cognition and behavior. It was also demonstrated that TDCS induces cortical excitability changes in the human motor cortex. The objective of this study was to analyze its possible benefit on gait disturbances in advanced Parkinson disease (PD) such as freezing of gait (FOG), apraxia and balance, which remain difficult to improve with subtalamic and pallidal deep brain stimulation.
Methods
Six PD patients, previously submitted to ablative surgery or DBS, with minor appendicular symptoms and severe gait disorder, underwent anodal TDCS over the leg representation in motor cortex. None had showed improvement of gait after levodopa trial. All patients were kept out of medications for at least 12 hours and submitted to 30' TDCS. Patients were assessed previously and up to 90 minutes after the stimulation. Outcome measure used Gait and Balance Scale (GABS).
Results
Four patients showed improvement of gait following TDCS superior to a 40% reduction in GABS. Two showed excellent response (reduction > 60%) and two moderate improvement of gait after TDCS. Only one patient did not respond to the stimulation.
Conclusions
In this pilot study, we observed a possible modulation of gait and balance after non-invasive motor cortex stimulation. TDCS should be investigated as new option in the assessment of gait disturbances in PD.

269 – Poster presentation

Utility of Eye Movement Tracking in the Differential Diagnosis of Movement Disorders

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Introduction
Differential diagnoses of movements disorders are often difficult, even for specialists in the field. Due to the purely subjective nature of clinical examinations, autopsy studies indicate that specialists only reach approximately 85% accuracy in clinical diagnoses, and 60% of movement disorder patients have their diagnosis changed at least once before death. Eye tracking, on the other hand, offers a non-invasive, quantitative method to objectively assess neurological function, with the potential to assist the clinician to derive at appreciably more accurate diagnoses.
Methods
Binocular eye movements were assessed in a large cohort of movement disorder patients with well-established diagnoses, using an Eyelink II binocular eye tracker while subjects followed random step displaced stimuli.
Results
Over 1,000 subjects with well-established diagnoses have been enrolled to date, and distinct abnormal eye movement patterns have been identified for numerous movement disorders (e.g. PD, ET, MSA, PSP, vascular parkinsonism, etc). Additionally, another 600 subjects have been assessed at initial consult to the clinic and show patterns consistent with those with established diagnoses. These findings suggest the ability of eye tracking to accurately differentially diagnose a patient at their initial visit to a specialist.
Conclusions
Eye tracking offers an objective method to assist clinicians in the differential diagnose of a wide variety of movement disorders. The implications are manifold in that more accurate diagnoses of movement disorders would be expected to improve surgical outcomes as a result of achieving more reliable selection of appropriate surgical candidates for such procedures as DBS and shunting for NPH.

270 – Poster presentation

Model-Based and Mirrored Coordinates for Optimal Spatial Distribution of Intrastriatal Neural Grafts

William Omar Contreras Lopez, Guido Nikkhah, Elisabeth Schültke, Luciano Furlanetti, Michael Trippel
São Paulo, Brazil, and Freiburg, Germany

Introduction
Intrastriatal neural transplantation using multiple grafts is an experimental approach to the treatment of Huntington's disease (HD). Brain atrophy makes stereotactic plans in these patients a tedious procedure with a risk of suboptimal spatial distribution of the grafts in transplantation procedures. Here we present our self-developed software to optimize the surgical stereotactic planning for bilateral neurotransplantation procedures. It allows close to symmetrical distribution of the stereotactic coordinates in relation to the mid-commissural point (MCP), proposing automatically the planning coordinates for the first transplanted hemisphere and mirrored coordinates to be used in the contra-lateral hemisphere.
Methods
Twenty-two consecutive HD patients underwent bilateral stereotactic striatal transplantation. Two caudate nucleus and four putaminal tracks were planned bilaterally. For the second, contra-lateral transplantation, the coordinates were mirrored in order to determine contralateral targets and trajectories. Intra-individual comparison between software given coordinates and finally used coordinates was performed.
Results
No statistical significance was found comparing a) the differences between coordinates proposed by the software and the final coordinates and b) the distribution of the transplantation sites in relation to the midline for the right vs. left hemisphere. No intra- or postoperative transplantation-related adverse events occurred.
Conclusions
The use of model-based and mirrored coordinates allowed optimal spatial distribution of the grafts. Minor changes were required comparing right to left coordinates giving proof-of principle. The initial use of the software suggests that it may be useful in experimental transplantation trials where neural cell grafts are to be implanted into predefined target sites in the human brain, whether unilateral or bilateral.

271 – Poster presentation

17.6T MR Microscopy Analysis of Deep Brain Stimulation Lead Locations in Parkinson's Disease

Takashi Morishita, Choong Hean Lee, Michael S. Okun, Stephen J. Blackband, Anthony Yachnis, VInata Vedam-Mai, Justin D. Hilliard, Kelly D. Foote
Gainesville, FL

Introduction
There are only few post-mortem brain studies of patients with previous deep brain stimulation (DBS) surgery, and most are histopathological and not magnetic resonance imaging (MRI) based. We aimed to correlate precisely defined microanatomic sites of brain stimulation with known outcomes of DBS using ultra high-resolution MRI (aka, MR microscopy, or MRM), and correlate the images with pathological findings.
Methods
We have scanned the subthalamic areas from three Parkinson's disease (PD) DBS patients (five hemispheres) with a 17.6 T MRI scanner. The brains were dissected based on anatomical landmarks including the anterior and posterior commissures, then the three dimensional images were obtained. We obtained T1-, T2-, and diffusion weighted imaging sequences with in-plane resolution of 19 µm. Hematoxylin and eosin (H&E) staining was performed.
Results
This MRM technique clearly delineated the basal ganglia structures in the subthalamic area. We observed that while subthalamic nucleus (STN) DBS in each of the three patients was effective, only one of five electrodes was located within the dorsolateral STN. Mild gliosis was observed on H&E staining slices surrounding the DBS tract, and this change was also shown on the MRM images.
Conclusions
Electrical stimulation of the STN and the surrounding fiber systems in the subthalamic area produces variably beneficial modulation of the malfunctioning motor network in Parkinson's disease. The findings from this study may shed light on questions regarding the mechanisms of action of DBS and improve our understanding of basal ganglia neuronal circuitry.

272 – Poster presentation

A New Quantitative Assessment of Postural Stability in Parkinson's Disease

Nicholas Brandmeir, Cheryl Brandmeir, James McInerney
Hershey, PA

Introduction

Postural instability and falling in Parkinson's Disease (PD) are a major source of morbidity. Gait and postural responses in PD are typically assessed with intense, specialized laboratory equipment often leading to patient refusal and drop out, resulting in significant selection bias and limitations to external validity. The Biodex automated balance assessment system (Biodex) can provide an objective, and precise assessment of postural instability in a routine physical therapy evaluation.

Methods

Consecutive patients presenting for deep brain stimulator (DBS) evaluation were assessed by a trained physical therapist as part of their standard work up. The assessment included the Berg Balance Inventory (Berg), the Timed-Up-and-Go Test (TUG), the UPDRS parts III and IV, and the Biodex sway index and fall risk assessments. Normal values for the TUG and Berg were taken from published literature; comparisons for the Biodex were made with 18 healthy volunteers.

Results

Sixteen patients were assessed over 6 months. Cutoffs chosen for Sway Index were 1.0 for the 'Eyes Closed Firm Surface (Firm),' 2.9 for the 'Eyes Closed Soft Surface (Soft),' and 1.5 for the 'Fall Risk (FR).' Using these values the sensitivities produced by the Firm, Soft, and FR were 88%, 94%, and 94% respectively. The specificities were 78%, 89%, and 83%. Combining the Firm and Soft tests yielded a sensitivity and specificity of 81% and 94%.

Conclusions

The Biodex Balance Assessment Sway Index provides a highly sensitive, specific and quantitative way to evaluate postural instability in PD patients. This test outperformed the Berg with its reported sensitivity and specificity of 74%. More study is needed to determine if these parameters improve with DBS. This could prove to be a new test that is more sensitive and specific for evaluating patients with PD as candidates for DBS.

273 – Poster presentation

Is There a Learning Curve Associated with iMRI DBS Electrode Placement?

Rushna Ali, Lisa Scarpace, Lonni Schultz, Jason M. Schwalb
Detroit, MI

Introduction

The ClearPoint system with intraoperative MRI is an increasingly popular method for DBS electrode placement as an alternative to frame-based stereotaxis with electrophysiologic confirmation. However, to date, there have not been any reports of DBS placement from centers other than UCSF, where it was developed.

Methods

We performed a retrospective analysis of 19 patients who underwent bilateral DBS electrode placement under iMRI guidance between July 2011 and February 2014. Two groups were defined as those patients who had surgery in the first year of the institution's experience (n=7) and those with surgery after one year of experience (n=12). A two sample t-test was done to compare the length of surgery.

Results

Of these 19 patients, 13 (68%) were male and 6 (32%) female. In fourteen (73.6 %) patients the indication for surgery was Parkinson Disease and dystonia in the remaining 5 (26.3%). Mean length of surgery for patients who had surgery in the first year of the institution's experience was 4.89 ± 0.55 (SD) hours versus 4.85 ± 0.72 (SD) hours for patients who had surgery after one year of experience. The difference in the mean length of surgery between the two groups was not significant (p=0.90).

Conclusions

So far, we have been unable to observe a learning curve associated with DBS electrode placement using intraoperative MRI. We did not find a significant difference between the lengths of surgeries performed in the first year that our institution began using this novel technique, compared to surgeries performed after the initial year. Delays were attributed to prolonged scan times to keep the SARs low, software, hardware and instrumentation malfunctions and subsequent efforts to troubleshoot these issues. Further analysis will examine pitfalls and accuracy. Hopefully, we can reach the 3.75 hours of mean operating time reported by the group responsible for pioneering this modality.

274 – Poster presentation

Multiple Target Deep Brain Stimulation for Holmes Tremor

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Istanbul, Turkey

Introduction

Holmes in 1904 described a tremor which resulted from the destruction of the rubrospinal tract. Later it was named Rubral tremor. Medical treatment is usually ineffective and most of the patients need surgical intervention.

Methods

This is a case report.

Results

This 11-year-old girl was admitted to the hospital in March 2003 with the diagnosis of right thalamic abscess. Stereotactic abscess drainage and antibiotics treated the abscess successfully. However, 4 months after the treatment she developed left sided upper extremity tremor and dystonic movements. She underwent a right-sided Vim DBS in October 2005. Her complaints decreased gradually in the following months. However, 3 years after the surgery, the dystonic movements begun to disturb her. So an additional DBS for right GPi was performed in December 2008. Her dystonia responded well to this second surgery. Today, 5 years after second surgery she has slight but non-disturbing dystonia in her left hand.

Conclusions

In Holmes' tremor, due to the tremor and dystonic components, both VIM and GPi should be the surgical targets.

284 – Poster presentation

The Human Pedunculopontine Nucleus: A Precise Anatomical and Neurochemical Description Using Immunohistochemistry and Stereotaxic Approach for DBS Implantation

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Quebec City, Quebec, Canada

Introduction

Since the first identification of the pedunculopontine nucleus (PPN) in 1909 by Jacobsohn and its more detailed description later in 1954 by Olszewski and Baxter, the delineation of tegmental structures and their terminologies have been a source of continual confusion. It was then unsurprising that controversies regarding PPN anatomical localization were raised in the neurosurgical community when this nucleus became a new promising target for the treatment of freezing of gait by DBS. Particularly worth noting is the marked variation encountered in the literature regarding the site of electrode implantation in the brainstem. Indeed, while all studies report electrode implantation in the PPN per se, some suggest a target localized in the caudal midbrain while others advocate an electrode implantation more caudally in the pons. Thus, detailed anatomical and neurochemical data on the human brainstem are deeply needed to clarify the positions of tegmental structures of interest for DBS.

Methods

Here, the application of an immunohistochemical approach for choline acetyltransferase (ChAT), a reliable marker of cholinergic neurons has allowed us to provide a precise anatomical description of the human PPN and surrounding structures in the sagittal plane.

Results

We detected the presence of a dense cluster of ChAT+ neurons that corresponds to the PPN pars compacta lying at the pontomesencephalic junction along the rostral surface of the superior cerebellar peduncle. Taking into account the different stereotactic approaches used in DBS literature, we provided a set of coordinates corresponding to the PPN.

Conclusions

These new immunohistological data obtained from post-mortem material on sagittal plane provide relevant anatomical basis to precisely localize the PPN and its surrounding structures. This allow the reevaluation of the exact position of DBS electrodes already implanted in the so-called PPN while providing a faithful anatomoclinical approach to determine which specific brainstem structures must be targeted to treat gait disorders by DBS.

102: Sunday, June 1, 2014, 11:24-11:34 am; GS #1
Mapping Episodic Memory in the Medial Temporal Lobe

Maxwell B. Merkow, John Burke, Ashwin G. Ramayya, James J. Evans, Ashwini Dayal Sharan, Michael J. Kahana, Michael Sperling
Philadelphia, PA

Introduction
Whereas patient-specific, cortical mapping methods exist for sensorimotor and language domains, no comparable tool is available to identify circuitry underlying the memory system. One such technique, direct cortical stimulation, produces transient modulation of local neuronal tissue. Moreover, the medial temporal lobe (MTL) is well known to play a key role in several processes necessary for lasting memories. We tested the hypothesis that direct cortical stimulation of MTL structures would cause selective, site-specific episodic memory deficits.
Methods
We administered a free-recall memory task to five patients undergoing phase II monitoring for intractable epilepsy. High-frequency stimulation was randomly applied via at sub-afterdischarge current levels for five-second trains in one of four conditions: sham; encoding; storage; retrieval. Latency to response and recall accuracy were the dependent variables of interest. Within-subject comparisons were made with parametric statistics across lists.
Results
No serious adverse events occurred during stimulation administration to entorhinal cortex and hippocampal sites. Current applied ranged from 1.75-17mA (0.75-16.7 $\mu C/cm^2$/phase). 4 of 5 patients showed a significant memory deficit associated with at least one of the stimulation conditions, and in 3 of 5 patients, this effect on memory was found in only one condition. Accuracy was altered more commonly than latency (3 versus 1 patient) and application during the encoding, storage, and retrieval phases all lead to at least one change in memory performance. We did not observe any enhancement of memory function with stimulation.
Conclusions
Although recent reports found that stimulation in the entorhinal cortex enhances memory performance, we found that repeated, five-second stimulation in the MTL leads to specific, transient memory impairments. Stimulation of the structures in the MTL is a promising tool for understanding, mapping, and preserving the circuitry underlying the memory system. Future research should better delineate the structure-function effects we report here and determine the clinical predictive capacity of this technique.

103: Sunday, June 1, 2014, 1:40-1:50 pm; PS #1
Network Dynamics of Functional Connectivity in Category-Specific Visual Naming

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Houston, TX

Introduction
The occipital face area, temporal pole and fusiform face area constitute the core "face" recognition network, while the lateral occipital cortex, posterior inferior temporal, and parahippocampal gyri are preferentially involved in object recognition. The network dynamics underpinning interactions between category specific visual substrates are still not well understood, due to the poor temporal resolution of fMRI techniques used to investigate these regions.
Methods
We collected ECoG data in 26 patients and utilized surface-based mixed effects multilayer analysis (SB-MEMA) to perform topologically accurate, statistically valid group level analysis. We then used amplitude envelope correlations (AEC) to evaluate inter-regional information flow between category-specific regions identified by SB-MEMA. Finally, by computing AEC between two time-lagged signals, we generated estimates of directed information flow during visual naming of these two categories.
Results
We identified similar and over-lapping category-specific activity in the ventral and lateral occipito- temporal cortices. Locations of peak activity in FFH and PH regions formed distinct antero-posterior and medio-lateral category-specific gradients, that have not been previously described. Pure category selectivity was noted only in the superior parietal gyrus (objects), the posterior superior temporal sulcus (faces), and the anterior temporal pole (faces). AEC revealed short intense connectivity between ventral and lateral occipital regions for faces, but longer connectivity overall for common objects. During common object naming, information flow (time-lagged correlations) was bilateral between LO and VT electrodes, likely representing signatures of bottom up and top down modulation of local processing. In contrast, face naming exhibited more unidirectional connectivity from LO to VT electrodes.
Conclusions
Category specificity of these regions follows not simply from the amplitude of local tuning curves for given stimuli, but also in its temporal profile and in the patterns of inter-regional activation. Our analysis may provide a method for modeling cortical processes critical to face/object recognition for use in neural prosthetics.

104: Sunday, June 1, 2014, 1:50-2:00 pm; PS #1

Pre-stimulus Oscillatory Activity Predicts Successful Memory Encoding in a Paired Associates Episodic Memory Task

Rafi Haque, Srikanth Damera, Sarah K. Inati, Kareem A. Zaghloul
Bethesda, MD

Introduction
Previous studies investigating the neural basis of episodic memory encoding have demonstrated increases in high frequency oscillations and decreases in low frequency oscillations following the presentation of items that were successfully encoded in memory. However, it remains unclear what role neural activity preceding item presentation plays in successful encoding, and therefore to what extent brain states are optimized for memory encoding prior to stimulus presentation.
Methods
To investigate this, we recorded human intracranial electrocorticography signals (ECoG) from 25 neurosurgical patients receiving subdural strip and grid electrodes for seizure monitoring who participated in a paired associates episodic memory task.
Results
We found significant increases in low frequency (2-15 Hz) and high frequency (45-400 Hz) oscillatory activity preceding study pair presentations when items were subsequently recalled. We localized these changes to the left dorsolateral prefrontal cortex and the left posterior temporal lobe.
Conclusions
These results suggest that a specific pre-stimulus spatiotemporal pattern of spectral activity can predict paired associates memory encoding and identify a possible control signal to improve memory performance based on electrophysiological intervention.

105: Sunday, June 1, 2014, 2:00-2:10 pm; PS #1

Learning in Primates is Associated with Prefrontal Cortex Network Destabilization

Benjamin L. Grannan, Wenhua Zhang, Ziv Williams
Boston, MA

Introduction
Learning requires individuals to make arbitrary associations between environmental stimuli and behaviors leading to reward. However, it remains unclear which changes in neuronal activity reflect an animal's internal representation of a new memory rather than changes in the animal's external environment. Using a novel learning task in primates and multiple-neuronal recordings, we identify a neuronal signal in the prefrontal cortex (PFC) that is specific to learning.
Methods
Multiple-neuronal recordings were obtained from the dorsolateral PFC of monkeys performing a novel associative learning task. The monkeys were rewarded with drops of juice if they correctly identified one of two images associated with a reward. The rewarded image and reward quantity were changed at random intervals such that a change in reward was either associated or not associated with learning. The firing rate, entropy, variance and spike cross-correlations of the recordings were analyzed before and after a switch in reward. Comparisons were then made between switches in which the animals were required to learn a new association and those in which they experienced a change in reward without learning required.
Results
Total of 50 neurons were recorded in two primates. During episodes of learning, few neurons (3/50) demonstrated a change in firing rate. In comparison, more neurons (17/50) demonstrated a change in firing variance, suggesting that neuronal responses became unstable when the monkeys needed to change their responses from a well-learned association to a new response. When no learning was required, a similar small number of neurons (3 and 5 out of 13) demonstrated a change in firing rate and variance, respectively. Minimal changes were noted in entropy or spike cross-correlations.
Conclusions
Our data suggest that destabilization of PFC neural activity is a principal neural signature of learning new associations. More importantly, changes in neuronal stability appear to reflect the animal's internal representation of learned associations.

106: Sunday, June 1, 2014, 3:40-3:50 pm; PS #1

Changes in GABA and Glutamate Concentrations in the GPi during Memory Tasks in Patients with Parkinson's Disease during DBS Surgery

David P. Darrow, Zoltan Nadasdy, Klevest Gjini, Robert J. Buchanan
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Introduction
Validation and investigation of cognitive and memory cerebral circuitry in humans is a challenging frontier. In-vivo microdialysis during deep brain stimulation surgery presents a unique opportunity to directly measure the dynamics of neurochemistry in an awake, participatory patient. The basal ganglia have been observed to be responsible for immediate feedback-contingent implicit memory formation through functional imaging studies and psychometric testing in normal subjects and in patients with Parkinson's disease (PD). Recently, the authors published the first results investigating the role of GABA and glutamate measured directly from the subthalamic nucleus (STN) in patients using the weather prediction task (WPT) and declarative memory tasks in PD patients during DBS surgery.
Methods
In vivo microdialysis of GABA and glutamate in the internal globus pallidus was performed in two patients suffering from Parkinson's disease during immediate-feedback weather prediction and declarative memory tasks separated by wash-out periods.
Results
GABA was observed to rise more than 70% from baseline during immediate-feedback WPT while glutamate demonstrated a 30% increase. During the declarative tasks, GABA and glutamate were found to fall or maintain concentration with respect to baseline.
Conclusions
These results are consistent with current knowledge about basal ganglia dysfunction in Parkinson's patients performing implicit memory tasks. We hypothesize that the striatal projections to GPi mediate the increase in GABA, and projections from the hyperactive STN to GPi mediate the increase in glutamate observed. Moreover, these findings further support the authors' previous results in the STN. While the data are preliminary, the study heralds the challenges of neurochemical validation of cognitive basal ganglia function, while providing invaluable practical knowledge and salient methodological updates for other researchers.

107: Sunday, June 1, 2014, 3:50-4:00 pm; PS #1

Medial to Lateral Transfer of Feedback Learning Signals in Human Prefrontal Cortex

Sameer A. Sheth, Garrett P. Banks, Matthew Kamal Mian, Shaun Patel, Emad N. Eskandar, Elliot H. Smith
New York, NY, and Boston, MA

Introduction
Rapid adaptation to a changing environment is integral for survival. Feedback, both internally and externally generated, plays a pivotal role in our ability to thrive in complex environments. One salient feedback signal, the feedback-related negativity (FRN), manifests as a change in the scalp EEG evoked potential 100 to 200 ms after a subject has registered a behavioral response, and is greatest on central EEG contacts. While EEG source localization and fMRI studies have broadly implicated the medial prefrontal cortex, and especially anterior cingulate cortex (ACC), as the generator of the FRN, direct evidence of its source is still debated.
Methods
We examined intracranial electrocorticographic (ECoG) signals in 6 patients undergoing monitoring for medically refractory epilepsy. Eight-contact depth electrodes were implanted through the mediolateral extent of prefrontal cortex (6 left hemisphere and 4 right hemisphere), ranging from lateral PFC (lPFC) to ACC, two areas implicated in generating the FRN. Recordings were acquired while patients performed a Stroop-like cognitive interference task with alternating feedback and non-feedback blocks.
Results
While the FRN was observed in feedback-triggered low frequency (< 40 Hz) potentials on both medial and lateral contacts in both hemispheres, the FRN in the high-gamma range (70 – 150 Hz) increased from lPFC to ACC contacts in both hemispheres. Examination of coherence among depth electrodes demonstrated information transfer from ACC to the lPFC. Partial directed coherence, Granger Causality, and conditional mutual information analyses were used to quantify transfer of feedback-related information from medial to lateral prefrontal cortex.
Conclusions
These human ECoG recordings directly implicate the ACC as the source of the FRN and describe an oscillatory mechanism for propagation of feedback-related information from medial to lateral prefrontal cortex. These results have notable implications for models of reinforcement learning and prefrontal mechanisms of cognitive control.

108: Sunday, June 1, 2014, 4:00-4:10 pm; PS #1
Microstimulation of the Human Substantia Nigra Alters Reinforcement Learning

Ashwin G. Ramayya, Gordon H. Baltuch, Michael J. Kahana
Philadelphia, PA

Introduction
Animal studies have shown that phasic bursts of substantia nigra (SN) dopaminergic (DA) neurons strengthen action-reward associations during reward-based learning, but their role in human learning is not known. We applied microstimulation in the SN of patients undergoing deep brain stimulation (DBS) surgery for the treatment of Parkinson's disease (PD) as they performed a reinforcement learning task. Although microstimulation is often applied during DBS to aid in clinical targeting, it has not been previously applied in association with a cognitive task.
Methods
Eleven PD patients volunteered to take part in this study (8 male, 3 female, age = 63 ± 7, mean ± S.D). During surgery, subjects performed a two-alternative probability learning task, where rewards were contingent on stimuli, rather than actions. We applied microstimulation following a subset of feedback trials through a tungsten microelectrode using a FHC Pulsar 6b microstimulator (bi-phasic, cathode phase-lead pulses at 90 Hz, lasting 500 ms at an amplitude of 150 µAmps and a pulse width of 500 µs).
Results
Subjects demonstrated decreased learning following reward trials that were accompanied by SN microstimulation, compared to reward trials without stimulation ($p = 0.029$). Subjects who showed large decreases in learning also showed an increased bias towards repeating actions following stimulation trials ($p = 0.006$); thus, stimulation may have decreased learning by strengthening action-reward associations, rather than stimulus-reward associations. Additionally, stimulation-related behavioral changes were most prominent when the microelectrode was positioned near putative DA neurons ($p = 0.04$).
Conclusions
These results demonstrate that it is possible to modulate human reinforcement learning by applying microstimulation near midbrain dopaminergic populations. Thus, targeted-microstimulation near these neuronal populations may prove useful in treating psychiatric disorders that feature pathological reward-based learning (e.g., addiction).

138: Tuesday, June 3, 2014, 11:26-11:36 am; PS #5
Different Neuropsychiatric Outcomes in Long-term Pallidal versus Subthalamic DBS for Parkinson Disease (PD)

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Calgary, Albera, Canada

Introduction
Previous work suggests that DBS is associated with deficits in verbal fluency in PD patients. Executive function has been less frequently reported, particularly comparing the 2 targets of DBS, globus pallidus (GPi) and subthalamic nucleus (STN).
Methods
All patients undergoing either GPi or STN-DBS for PD in Calgary were assessed using a neuropsychological battery including IQ (WAIS-3), Beck's Depression Inventory II (BDI-II), Wisconsin Card Sorting Task (WCST) and verbal fluency at baseline and 1 year post-op. In addition, clinical assessments were conducted at the same timepoints using the Unified Parkinson's Disease Rating Scale (UPDRS) both off and on medication and/or stimulation.
Results
62 patients were available for analysis (12 GPi, 50 STN). Of these, 4 GPi-DBS patients had incomplete data, while another 4 patients are scheduled for follow-up in the next months. Thus, pre- and post-op data were available for 4 GPi-DBS patients, who were matched for age at time of surgery, gender, education and IQ with 4 STN-DBS subjects. GPi-DBS in comparison to STN-DBS was associated with more errors ($t=3.815$, $p=0.009$) and fewer conceptual level responses ($t=3.739$, $p=0.01$) on the WCST. Moreover, both groups exhibited reduced verbal fluency in the categorical subfield ($t=4.341$, $p=0.005$), and decreased UPDRS scores (off meds vs. off meds/on stim; $t=2.840$, $p=0.03$) relative to baseline, though no between-group differences were observed in these latter measures.
Conclusions
In this preliminary analysis, PD patients undergoing pallidal DBS had evidence of reduced executive function 1 year post-op relative to patients undergoing STN-DBS. In addition, both groups demonstrated some evidence of reduced verbal fluency concomitant with improved clinical function relative to baseline. These findings will be confirmed in a larger subset of patients.

275 – Poster presentation

A Population Spatial Probability Map of Essential Language Sites from Cortical Stimulation Mapping

Nitin Tandon, Thomas Pieters, Vatche Baboyan, Christopher R. Conner
Houston, TX

Introduction

Cortical stimulation mapping (CSM) – is the gold standard technique for localization of eloquent language sites (ELS). Despite its widespread use for several decades, these data are typically represented schematically, referenced to cortical surface landmarks. This has precluded the creation of useful population maps to generate apriori predictive models of the probability of language in specific cortical sites.

Methods

61 patients scheduled for intra-operative (awake craniotomy) or extra-operative (implanted subdural electrodes) language mapping, underwent pre-operative hi-resolution anatomical data acquisition at 3T. Mesh models of individual pial surfaces were generated. Each subject's spherical mesh was warped to to align with the folding patterns of a population averaged brain, to generate a standardized mesh with invariant node numbers. Language sites were localized using object naming with both auditory and visual cues, and an auditory repetition task. Stimulation currents ranged from 3-10 mA. Sites of stimulation associated with (positive-sites) and without (negative-sites) disruption of language were localized on the pial mesh-model using intra-op video and in-house software. A model of cortical depolarization by direct current spread in the human brain, fitted by experimental data from stimulation of primate cortex, was computed. The point probability of the presence of linguistic function for the entire cortex per subject was estimated.

Results

615 positive and 1089 negative ELS were localized. Population maps for each subtype of language function were generated. ELS were found to be densely clustered in the SFG, posterior STG and Wernicke's area, Broca's area and the fusiform gyrus.

Conclusions

We show that there is indeed a great degree of overlap in essential language sites. Spatial probability maps of language allow for direct comparison of CSM data with functional imaging and lesion analysis. Additionally, such maps allow for empiric estimates of risk to language during cortical resections.

276 – Poster presentation

Brain Atrophy after Whole-Brain Radiation Therapy Plus Radiosurgery versus Radiosurgery Alone for Metastatic Lung Cancer

Stephanie Chen, Edward A. Monaco III, David Michael Panczykowski, Ajay Niranjan, Hideyuki Kano, L. Dade Lunsford
Pittsburgh, PA

Introduction

Whole-brain radiation therapy (WBRT) has been the reflexive treatment of patients with brain metastases. However, there is growing evidence that WBRT has significant neurotoxic side effects including leukoencephalopathy and neurocognitive dysfunction. Linear measures of brain atrophy including the bifrontal index and bicaudate ratio have been identified as reliable markers of brain atrophy in neurocognitive disorders. This study uses these measures to assess the risk of brain atrophy after WBRT plus stereotactic radiosurgery (SRS) as compared to SRS alone for the treatment of brain metastases from lung cancer.

Methods

We retrospectively compared 13 patients with non-small cell lung cancer brain metastases who underwent WRBT plus SRS to 16 patients who had only SRS. All patients survived at least 1 year after treatment. Linear measures of brain atrophy (bifrontal index and bicaudate ratio) were made from MRI images performed at the time of initial therapy, and approximately two years after therapy. Bifrontal index (BFI) was measured as the maximal width between the tips of the frontal horns of the lateral ventricles divided by brain width along the same line. Bicaudate ratio (BCR) is the minimum intercaudate distance divided by brain width along the same line.

Results

Baseline measures of brain atrophy were similar at the time of initial therapy. Patients treated with WBRT and SRS had significantly greater increases in BFI ($p < 0.03$) and BCR ($p < 0.004$) two years after treatment compared to patients who underwent SRS alone.

Conclusions

Risk of cerebral atrophy in patients treated with SRS alone for brain metastases was significantly lower than for patients treated with WRBT plus SRS as measured by BFI and BCR. These data add to mounting evidence that SRS therapy for brain metastases avoids the delayed toxicity of WBRT. Thus, clinicians may wish to rethink the reflexive upfront utilization of WBRT.

277 – Poster presentation

Stimulus Dependence of Gamma Oscillations in Human Visual Cortex

Kai Miller, Dora Hermes, Brian Wandell, John Winawer
Stanford, CA

Introduction

A striking feature of some field potential recordings in visual cortex is a rhythmic oscillation within the gamma band (30-80 Hz). These oscillations have been proposed to underlie computations in perception, attention, and information transmission. Recent studies of cortical field potentials, including human electrocorticography (ECoG), have emphasized another signal within the gamma band, a non-oscillatory, broadband signal, spanning 80-200 Hz. It remains unclear under what conditions gamma oscillations are elicited in visual cortex, whether they are necessary and ubiquitous in visual encoding, and what relationship they have to non-oscillatory, broadband field potentials.

Methods

ECoG was measured from early visual areas (V1/V2/V3) while different types of simple visual stimuli were shown to patients (luminance gratings, noise patterns, and natural images). The ECoG signal was analyzed for simple oscillations as well as broadband changes.

Results

We demonstrate that ECoG responses in human visual cortex can include robust narrowband gamma oscillations, and that these oscillations are reliably elicited by some spatial contrast patterns (luminance gratings) but not others (noise patterns and many natural images).

Conclusions

So-called "gamma oscillations" are an idiosyncratic finding in brain signals. The gamma oscillations can be conspicuous and robust, but because they are absent for many stimuli which observers can see and recognize, the oscillations aren't necessary for seeing. In contrast, all visual stimuli induced broadband spectral changes in the ECoG response. Asynchronous neural signals in visual cortex, reflected in the broadband ECoG response, can support transmission of information for perception and recognition in the absence of pronounced gamma oscillations.

278 – Poster presentation

Human Substantia Nigra Neurons Encode Decision Outcome and Categorization Uncertainty in an Auditory Categorization Task

Robert Allen McGovern, Andrew Kai-Hong Chan, Charles B. Mikell, John Paul Sheehy, Vincent P. Ferrera, Guy M. McKhann
New York, NY, and Phoenix, AZ

Introduction

The ability to categorize a sensory stimulus is a decision making process that requires attention to the relevant stimulus dimension, comparison of the stimulus to a category boundary, and selection of an appropriate response. This ability depends on the certainty one has in placing the stimulus into a category. Here we report the behavior of putative dopaminergic (DA) neurons in the human substantia nigra (SN) during an auditory decision-making task.

Methods

We used single neuron extracellular recordings in awake human subjects undergoing surgery for Parkinson disease. While recording from the SN, subjects were asked to classify pure tones, selected from a predetermined range of frequencies, as either low- or high-pitched relative to an explicit threshold tone.

Results

We recorded from 34 putative DA neurons. During a period 50-500 ms after tone onset, but prior to subject response, DA neuron firing rate was significantly correlated with increasing level of uncertainty (i.e. tones closer to threshold) ($p=0.04$) and correctness of outcome (i.e. correct categorization) ($p=0.03$). The firing rate of non-DA neurons ($n = 23$) did not show a significant correlation with either uncertainty or outcome.

Conclusions

During categorical decision-making, putative DA neurons in human SN carry signals that are predictive of decision outcome (correct, incorrect) and are sensitive to uncertainty. Neuronal activity was highest during difficult (uncertain) decisions that resulted in correct responses and lowest during easy decisions that resulted in incorrect responses. These results suggest that DA neurons in the SN signal the subject's degree of attention to the task.

101: Sunday, June 1, 2014, 11:14-11:24 am; GS #1
Evolution of Microendoscopic-guided Percutaneous Cordotomy for Intractable Pain: Case Series of 24 Patients.

Erich Talamoni Fonoff, William Omar Contreras Lopez, Ywzhe Sifuentes Almeida de Oliveira, Manoel Jacobsen Almeida de Oliveira Teixeira
São Paulo, Brazil

Introduction
Percutaneous anterolateral cordotomy is currently performed under indirect X-ray visualization (fluoroscopy or CT). In 2010, the authors proposed a new technique involving the use of an intradural endoscope for direct visualization of the spinal cord through a percutaneous approach. Herein, the authors describe a series of 24 patients who received a cordotomy using such technique.
Methods
Twenty-four adult patients with intractable cancer pain were treated by means of endoscopic-guided percutaneous radiofrequency cordotomy, using double-channel endoscopic technique. The procedure was performed under local anesthesia. Initially a percutaneous lateral puncture was performed under fluoroscopy guidance to localize the target (spinal canal in C1–C2 interspace). As soon as subarachnoid space was reached by the guide cannula (17-gauge needle), the endoscope was inserted for visualization of the spinal cord and surrounding structures. The target for spinal cord puncture was established as the midpoint of the distance from the dentate ligament and the ventral root entry zone. After right visualization of the target a second needle was inserted to guide the radiofrequency electrode. Cordotomy was performed by a standard radiofrequency method.
Results
The endoscopic double-channel approach achieved a clearly neuroanatomical visualization of the target in 91% of the cases. This translated into satisfactory postoperative outcome, reaching analgesia in the region in more than 90% of the cases. Two patients developed transient ataxia lasting few weeks until total recovery.
Conclusions
This series demonstrates that the use of percutaneous endoscopic cordotomy with the double-channel technique is useful for particular manipulation of the spinal cord, adding a degree of safety to the procedure.

109: Sunday, June 1, 2014, 1:40-1:50 pm; PS #2
Is Insertional Effect a Predictor of Long-term Success after Deep Brain Stimulation for Neuropathic Pain?

Ido Strauss, Vibhor Krishna, Clement Hamani, Soha Abdu Alomar, Andres M. Lozano
Toronto, Ontario, Canada

Introduction
Central neuromodulation can be used in selected cases for chronic intractable pain. We have observed acute pain relief in some patients with mere electrode insertion into the sensory thalamus and/or periventricular gray (PVG) . This phenomenon is termed as insertional effect. A trend towards successful outcome after DBS was previously reported.
Methods
We identified patients who underwent deep brain stimulation procedure for the treatment of neuropathic pain at our institution. A retrospective chart review was performed to abstract clinical history, occurrence of insertional effect and long-term outcomes. Successful outcome was defined as pain relief at last follow-up either due to active stimulation or insertional effect.
Results
We identified 36 patients (mean age 53±13 years) who underwent DBS at our institution from 1994-2013. The most common pain syndromes were post stroke pain (39%), post-traumatic pain (19%). All patients underwent thalamic (Vc) DBS (unilateral in 91.7%). Additional PVG electrode was inserted in 17 (47.2%) patients. Insertional effect was observed in 19 patients (52.3%) with majority reporting short-term insertional effect (18/19) lasting from 2 weeks – 7 months. One patient had a prolonged insertional effect, and is still pain free for over 11 years. At the last follow-up 6 patients reported satisfactory pain relief from active stimulation and 2 patients reported pain relief from insertional effect (successful outcome in 8 patients, 22.2%). Seven out of 19 patients who experienced insertional effect had long-term successful outcomes while only 1 patients without insertional effect was categorized as successful outcome (Fischer's exact test, two tailed $p = 0.047$).
Conclusions
Insertional effect after DBS is a significant predictor of long-term pain control. The underlying mechanism is poorly understood but could involve lesioning or disruption of pain mediating neural elements. The high prevalence and predictive significance of insertional effect should be taken into account in future studies.

110: Sunday, June 1, 2014, 1:50-2:00 pm; PS #2

Prospective Study of Patient Outcomes Following Spinal Cord Stimulation with Intraoperative Monitoring

Steven G. Roth, Joannalee C. Campbell, Jessica Haller, Meghan Heran, Priscilla De La Cruz, Steven Paniccioli, Michael Briotte, M. Reid Gooch, Julie G. Pilitsis
Albany, NY

Introduction
Spinal Cord Stimulation (SCS) is a well-established modality to treat chronic pain associated with failed back surgery syndrome (FBSS) and complex regional pain syndrome (CRPS). Traditionally, SCS was performed awake, but many clinicians are now performing SCS asleep with intra-operative monitoring (IOM). There is little evidence in the literature on the value of IOM. We present a prospective study of patients undergoing SCS with IOM and compare to historical outcomes from awake procedures.
Methods
66 patients underwent permanent SCS placement for diagnoses including FBSS (27), CRPS (17), failed neck surgery syndrome (6), and radiculitis/neuropathy (17). IOM consisted of triggered electromyography (EMG) and somatosensory evoked potential (SSEP) collisions. IOM data were compared to device usage information obtained at follow-up. Objective outcomes were tracked through serial administration of the Oswestry Disability Index (ODI), Beck Depression Inventory (BDI), Pain Catastrophizing Scale (PCS), McGill Pain Questionnaire (MPQ), and pain Visual Analog Scale (VAS).
Results
22 patients reached 6-month follow-up. Statistically significant ($p < 0.05$) improvements were present (mean+/-SE) in ODI (54.9%+/-3.0% to 46.1%+/-3.7%), PCS-Rumination (9.8+/-0.9 to 6.6+/-1.1), PCS-Helplessness (11.3+/-1.1 to 6.2+/-1.2), PCS-Total (25.7+/-2.4 to 15.8+/-2.7), and pain VAS (6.8+/-0.3 to 4.9+/-0.5). (Figure 1, 2, 3) Results were similar to 2008 PROCESS study, where a cohort of 42 FBSS patients showed significant improvement in ODI (approximately 59% to 46%) and leg pain (VAS; approximately 7.8 to 4.3) at 24 months post SCS implantation. Appropriate lateralization was demonstrated by EMG in 82% of cases. When specific contacts elicited EMG responses in appropriate painful areas (n=14), these contacts and/or those immediately adjacent were in use for 86% of cases at follow-up.
Conclusions
To date, our prospective study demonstrates significant improvement in pain and disability in patients undergoing SCS using IOM for a variety of indications. IOM has the additional advantage of helping to streamline programming.

111: Sunday, June 1, 2014, 2:00-2:10 pm; PS #2

High Frequency Stimulation in the Dorsal Column – Blockade of Na^+ Conductance Related to Subtle Differences within the Subcomponents of the h-Gate

Jeffrey E. Arle, Longzhi Mei, Kristen W. Carlson, Jay L. Shils
Boston, MA, and Burlington, MA

Introduction
With regard to putative mechanisms of using high frequency (HF) in spinal cord stimulation, we have examined, from a computational standpoint, the idea that axons may in fact be affected by HF stimulation but that examination of such effects needs to be explored at the level of conductance channel gate subcomponents and dynamics and on a very rapid time scale. Examination was made in an active axonal model using steady square-wave input from 50 Hz up to 10 kHz.
Methods
An active axonal model based on some of the previously published parameters was created and adjusted to compensate for publication errors and dynamics that matched those found in similar models within the literature. Extensive analysis of inputs from 50 Hz-10 kHz, fiber diameters from 5.7µm-14µm, and m-, h-, and n-gate dynamics at the level of alpha- and beta-subcomponents were explored over a typical computed timeframe of 500ms at time steps of 0.01ms.
Results
Complete or nearly complete block of Na^+ conductance occurred above approximately 8kHz, though the frequency where the block began varied. The variability of the block threshold varied based most sensitively on h-gate dynamics and adjustments in beta(h). Such adjustments altered the time constant of the h-gate and thus the inactivation of the channel. At higher frequencies, it appeared that the channel was incapable of opening and closing and allowed no ionic flux. Importantly, larger diameter fibers were more likely blocked or blocked at lower frequencies from this phenomenon.
Conclusions
HF may be able to provide SCS pain relief without paresthesia and over wider topographies because larger fibers are blocked enough to eliminate paresthesia, and far more smaller diameter fibers can be activated at lower levels of stimulation, ultimately inhibiting WDR neurons broadly.

112: Sunday, June 1, 2014, 3:40-3:50 pm; PS #2

Trigeminal Neuralgia from Multiple Sclerosis: Is Percutaneous Surgery Effective?

Imran Noorani, Girish Vajramani, Amanda Lodge, Owen Sparrow
Southampton, UK

Introduction

Trigeminal neuralgia (TN) is commoner in patients with multiple sclerosis (MS). Percutaneous surgery is an established treatment for TN. However, it is not known if such surgery is as effective for TN in those with MS.

Methods

A retrospective review was undertaken of all consecutive glycerol rhizolysis, thermocoagulation and balloon compression procedures in a single centre between 1994 and 2013. For analysis, patients were divided into those with MS and without MS.

Results

339 percutaneous procedures were performed in non-MS patients (134 glycerol rhizolyses, 136 thermocoagulations, 69 balloon compressions), 138 of whom were males and 201 were females. 62 procedures were performed in MS patients (19 glycerol rhizolyses, 28 thermocoagulations, 15 balloon compressions), comprising 23 males and 39 females. The follow up ranged from 3 months to 16.7 years for glycerol rhizolysis and thermocoagulation, and 3 months to 3 years for balloon compression. The mean age of MS patients was 61 years and that of non-MS patients was 73 years. For non-MS patients 3 months after a procedure: 60.4% were pain free off medication,17.9% were pain free with medication, 10.5% had partial relief, and 11.2% had no relief. In the MS group, 55.4% were pain free off medication, 17.9% were pain free on medication, 17.9% had partial pain relief, and 8.9% had no relief. The complication rate was 25% for MS and 36% for non-MS patients. Median time to pain recurrence was 14 months (standard error 2.4 months) for MS and 18 months (standard error 2.8 months) for non-MS. Kaplan-Meier analysis demonstrated no significant difference in long-term pain relief duration for MS and non-MS patients ($p = 0.505$, log-rank test).

Conclusions

Percutaneous surgery is safe and effective for trigeminal neuralgia in those with multiple sclerosis, with similar long-term pain relief duration as for those patients not suffering from multiple sclerosis.

113: Sunday, June 1, 2014, 3:50-4:00 pm; PS #2

Epipulse-retro: Retrospective Study on Epidural Pulsed High Frequency Stimulation (500 000 Hz) in Pain Therapy

Frank Hertel
Luxemburg

Introduction

Epidural pulsed high frequency stimulation (EPRF) has been introduced as a non lesioning procedure for pain treatment. So far, there is no clinical data available.

Methods

We retrospectively analysed a consecutive series of 136 patients at 3 institutions with a follow-up of 10 months. The patients were suffering from different kinds of pain longer than 3 months (up to several years).

Results

The patients were treated under local anesthsia with a different number of impulses, each for 4 min, bursts of 480 msec (frequency 500 kHz) and a temperature below 42^{o} C. The additional influence of drugs was ruled out, so that the effects were due to stimulation alone. More than 60% of patients were satisfied or somewhat satisfied. Drug intake and invasive treatments could be significantly reduced. The stimulation sites were all inside the spinal canal, but with a wide variety (nerve root exit zone, posterior medullary fibres) between the levels of C2 and the lower lumbar region. We had no serious complications except for 3 temporary CSF leaks. There were no infections and no neurological deficits.

Conclusions

This is the first published clinical study on EPRF treatment. EPRF is a new treatment for chronic pain. It seems to be effective and safe. We did not find any sign or hint for lesions. Our study supports the hypothesis, that EPRF is a non-lesioning procedure. The study could not analyze the most effective stimulation site, nor the most effective stimulation parameters.

114: Sunday, June 1, 2014, 4:00-4:10 pm; Par #2

The Nucleus Accumbens as an Adjunctive Target for Deep Brain Stimulation in Central Post-Stroke Pain

Prakriti Gaba, Grant William Mallory, Deborah A. Gorman, Squire M. Stead, Bryan T. Klassen, Paola Sandroni, James Watson, Kendall H. Lee
Rochester, MN

Introduction

Deep brain stimulation (DBS) is a widely accepted therapy for a variety of neurologic disorders. However, results of DBS for chronic pain have been variable. Classically, the periaqueductal and periventricular gray (PAG/PVG) regions, and the ventralis caudalis of the thalamus have been the primary targets, alone or in combination. An NIH prospective study of a new target (the Nucleus Accumbens (NAC), led by A. Machado) is currently underway. Recently, we implanted NAC and PAG/PVG electrodes in two patients for central poststroke pain (CPSP) and now present extended follow-up.

Methods

Visual analog pain scale (VAS) scores prior to implantation and the perioperative period were compared to follow-up VAS scores at various time points. A formal pain disability index (PDI) and a patient satisfaction questionnaire were also evaluated.

Results

Short term results at one year demonstrated a marked reduction in VAS scores (mean preoperative VAS = 9 vs. mean postoperative VAS=4). At greater than 2.5 year follow-up, one of the two patients continues to have significant benefit with maintained reductions in VAS ratings (a VAS score of 5) and a significant reduction in PDI from 46 to 29 out 70. The other patient experienced a subsequent stroke that has resulted in further debility and a recurrence in pain between follow-up intervals. Both patients expressed overall satisfaction with surgery, saw a significant improvement in activities of daily living, home responsibilities and social interaction, and would have undergone the procedure again.

Conclusions

The NAC may be an effective adjunctive target for CPSP. Improvements were seen with respect to PDI and VAS at 1 and 2.5 year follow-up in both patients, with one patient showing sustained benefit at greater than 2.5 years after surgery. While the overall efficacy of combined NAC and PVG stimulation for CPSP is not known, further investigation is warranted.

139: Tuesday, June 3, 2014, 11:36-11:42 am; PS #5

Combined Occipital and Supraorbital Nerve Stimulation for Chronic Migraine

Shannon W. Hann, Chengyuan Wu, Ashwini Dayal Sharan
Philadelphia, PA

Introduction

Occipital nerve stimulation (ONS) has been studied in a few clinical trials for the treatment of chronic migraine (CM) with failure to prove sufficient efficacy. To date, peripheral nerve stimulation (PNS) for the treatment of primary headache is limited to off-label use only. The authors report their institutional experience in CM therapy with combined ONS and supraorbital nerve stimulation (SONS).

Methods

Fourteen patients treated with dual ONS and SONS for CM were studied with follow-up ranging from 3 to 60 months.

Results

Seventy-one percent achieved successful stimulation as defined by a 50% or greater decrease in pain severity. The mean reduction in headache-related visual analog scale (VAS) score was 3.92 ± 2.4. Half of the patients also had resolution of migraine-associated neurological symptoms and returned to normal functional capacity. The main adverse events included lead migration (42.8%), supraorbital lead allodynia (21.4%), and infection (14.2%) with a resulting high reoperation rate (35.7%). The authors' stimulation efficacy was superior to the combined 33% positive response rates (= 50% pain reduction) in the published studies of ONS for CM.

Conclusions

Dual ONS and SONS therapy for chronic migraine in our institution showed improved pain reduction and quality of life in patients compared with ONS or SONS alone. This is likely due to the fact that topographical paresthesia induced by combined ONS and SONS covers the area of migraine pain better than ONS alone. Well constructed randomized controlled clinical trials in the future will be needed for wider acceptance of PNS for primary headache.

279 – Poster presentation

Wide Dynamic Range Neuron Inhibition as a Function of Fiber Diameter, Firing Rate, and Topography – Potential Relevance to High Frequency Stimulation

Jeffrey E. Arle, Kristen W. Carlson, Longzhi Mei, Jay L. Shils
Boston, MA, and Burlington, MA

Introduction

High frequency (HF) paradigms for spinal cord stimulation pain relief, usually thought to be between 1kHz and about 10kHz, has been thought to provide wide-topographic benefit using sub-paresthesia stimulus levels. Whether HF is effective and what its mechanisms may be remains unclear. Two theories predominate: 1) there is a type of axonal blockade within dorsal column fibers that somehow limits pain transmission, though these fibers are not known to carry neuropathic pain signals, or 2) either blockade or activation from HF stimuli in dorsal column fibers leads to dynamic inhibition within the cord or brain circuitry that mitigates pain processing. We have addressed the second theory in this work.

Methods

We have used a large scale, dynamic circuitry model of the spinal cord previously published for assessing the potential for retrograde dorsal column fiber stimulation to lead to inhibition of WDR cells within the cord, as well achieving differential inhibition of neuropathic pain signals over nociceptive pain signals. The model was then evaluated using a variety of topographic distributions of Ia fiber inputs at lower firing rates to determine the dorsal horn neural dynamics and WDR activity.

Results

WDR cells are significantly and widely inhibited even by low firing rates of Ia fibers if the breadth of topography represented by those fibers is broad enough. Inhibition was to a similar degree as if typical distributions of fibers were used at higher firing rates as would be expected with typical clinical parameters of DCS.

Conclusions

WDR inhibition may be the hallmark of the typical mechanism of benefit using SCS. HF stimulation at subthreshold levels may provide a wider topographic range of low-level firing. These results suggest results of pain relief could be similarly achieved with such HF paradigms.

280 – Poster presentation

The Predictive Power of Balloon Shape on Outcome of Percutaneous Balloon Compression for Trigeminal Neuralgia

Tiago da Silva Freitas, Fernanda Albernaz Valente, Oswaldo Marquez Neto, Louise Christine Santos, Fernanda Villas Boas Araújo
Brasilia, Brazil

Introduction

Percutaneous balloon compression is a simple and effective treatment of trigeminal neuralgia with the special advantage of being the only percutaneous technique that can be simply performed with the patient under general anesthesia. The results between and within different series are varying, and different parameters have been described as outcome predictors. The objective of this study is to evaluate one isolated parameter: the balloon shape and its influence on the outcome and disease control in essential trigeminal neuralgia (TN)

Methods

We studied prospectively 82 patients who were submitted to percutaneous balloon compression with diagnosis of unilateral TN from 2006 – 2009 at the Functional Neurosurgery service from the University Hospital of Brasilia (HUB). Clinical follow-up and intraoperative radiographs from these patients were analyzed and the balloon shape parameters were categorized. Univariate and multivariate analyses were performed to correlate this surgical parameter to pain relief.

Results

The balloon shape had a significant impact on initial response and on time to recurrence of pain. A pear-shaped balloon resulted in a far better surgical result than a non pear-shaped balloon ($p < 0.004$). The difference between a distinct and a less distinct pear shape was not significant ($p = 0.14$).

Conclusions

The authors have demonstrated that using a pear-shaped balloon when performing percutaneous balloon compression for trigeminal neuralgia results in longer pain relief than non–pear-shaped balloons.

281 – Poster presentation

Subdural Motor Cortex Stimulation for Medically Intractable Face Pain

Grant William Mallory, Jan T. Hachmann, Matt Stead, Paola Sandroni, Kendall H. Lee, Daniel A. Clayton, Deborah A. Gorman, Bryan T. Klassen
Rochester, MN, and Seattle, WA

Introduction

Motor cortex stimulation has been used for pain syndromes. Most studies involve small cohorts, varying surgical technique (epidural versus subdural implantation), lack of long-term follow-up, and heterogeneity with respect to pain syndromes. Thus little is known about the overall efficacy in individual disorders or whether subdural or epidural stimulation is more effective. We report long-term outcomes in patients undergoing subdural motor cortex stimulation for intractable neuropathic face pain.

Methods

Operative logs were searched for patients undergoing subdural motor cortex stimulation at Mayo Clinic Rochester between January 2007 and December 2013. Medical records were reviewed for baseline demographics, preoperative pain features, and complications. Primary outcome measures included mean reduction in Visual Analog Scale (VAS) scores, change in medication use, and responses on a standardized mail-out and telephone quality-of-life questionnaire.

Results

Mean age at implant was 51 years ±11 years, and mean follow-up was 37.4 months (range 5.3 to 75.2). Twenty three of 24 patients (96%) responded favorably to trial stimulation. Long term outcomes were available in 20 out 24 patients (88%). Two patients were excluded for refusal to participate in the study; two patients were lost to follow-up. The mean reduction in VAS scores was 3.5 (range 1 to 7). Seven patients (35%) were able to wean off medication entirely. Overall satisfaction with surgery and willingness to undergo surgery again was reported by 90% of patients. Four patients experienced post-operative hemorrhage requiring surgical evacuation, and one experienced surgical site infection. Seizures limited to the a period immediately following re-programming were reported in six. No permanent morbidity or mortality resulted from these complications.

Conclusions

Subdural motor cortex stimulation is an effective therapy for medically intractable face pain. Further study is necessary to better ascertain the true incidence of complications and whether it is more effective than epidural stimulation.

282 – Poster presentation

Peripheral Nerve Stimulation for Neuropathic Pain Caused by Leprosy: One Year Follow-Up

Tiago da Silva Freitas, Lucas Garcia de Souza Godoy, Carlos Gilberto Fávero Jr, Robercon Alves Carmo, Hugo Souza Mota Moreira, Iruena Moraes Kessler
Brasilia, Brazil

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 leprous neuropathy.

Methods

18 leprosy patients with chronic neuropathic pain irresponsive to medication and surgical decompression were selected for a trial implant. All patients underwent prior testing for 7 days and were assessed with Visual Analog 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 3 months, 6 months and 1 year post-procedure.

Results

9 patients received a permanent device. Among these, 6 patients (75%) showed at least a 50% improvement in VAS and NPS while 3 patients showed a 30% scale improvement. All improvements maintained during 1 year follow-up. There were 2 lead migration and no infection

Conclusions

Leprosy remains a public health problem in developing countries and is a major cause of peripheral neuropathy worldwide. Peripheral nerve stimulation is an important additional tool in a long term management of chronic neuropathic pain secondary to leprosy.

283 – Poster presentation

Typical Trigeminal Neuralgia Patients with Axonal Degeneration and Amyloidosis - Report of Two Cases

Jie Ren, Guoming Luan
Beijing, China

Introduction
Demyelination of the root entry zone of the trigeminal nerve seems to be a major cause of trigeminal neuralgia (TN). Two typical TN patients were investigated by trigeminal nerve biopsy during cerebello-pontine angle exploration surgery, which revealed pathological changes.
Methods
Patient 1: a 63-year-old woman presented with drug resistant left TN. She had a 4-year history of lancinating pain paroxysms in the second and third trigeminal branches. Microvascular decompression was performed one year before she was admitted to our hospital, and did not relieve the pain. Re-operation was performed by exploration of the cerebello-pontine angle. Patient 2: a 71-year-old woman also presented with left classical TN. She had a half-year history of lancinating pain in the second trigeminal branch and was drug resistant. Exploration of the cerebello-pontine angle was also performed. There was no vascular compression of the trigeminal nerve in both patients. Then, partial rhizotomy was performed at the root entry zone and the biopsy sample was processed for light and electron microscopy. The effectiveness of operations was evaluated during follow-up period.
Results
Patient 1: GFAP stain showed root entry zone of the trigeminal nerve. Pathologic changes in the biopsy included amyloidosis especially in the central part, axonal degeneration and no obvious demyelination. Axon changes include vesicular corpuscles and dense granules; no inflammatory cells were present. Patient 2: swelling of the axons and amyloidosis. Complete relief of the symptoms was achieved in both patients with mild facial numbness after the procedure.
Conclusions
Trigeminal neuropathy appears to be the most convincing explanation for the occurrence of pain. Although compression injury to the trigeminal root leading to demyelination is a major reason in the pathogenesis of TN, axonal degeneration was another pathological change especially in those without vascular compression. TN in older women may be associated with this kind of causes.

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