
Neuromodulation: Technology at the Neural Interface
Syllabus
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December 9- 12, 2007
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international neuromodulation society
8th world congress
North American Neuromodulation Society
est. 1994
11th annual meeting

SUNDAY DECEMBER 9, 2007

0800 – 1200 Princesa Ballroom B-C (13)
Plenary Session: Brain Day
Ali Rezai, MD, Session Chair
Cleveland Clinic
Center for Neurological Restoration, Director
Cleveland, Ohio USA

0800 – 0840 Princesa Ballroom B-C (13)
Keynote Address - see Non-CME Syllabus for information
Alan Levy, PhD
Northstar Neuroscience
Seattle, Washington USA

0840 - 0920 Princesa Ballroom B-C (13)
MRI Safety Issues for Implantable Neuromodulation Devices
Frank G. Shellock, PhD
Adjunct Clinical Professor of Radiology and Medicine
Keck School of Medicine
Director for MRI Studies of Biomimetic MicroElectronic Systems
University of Southern California
Los Angeles, California USA

Abstract
A patient with an electrically, magnetically, or mechanically activated implant is typically excluded from examination by MRI unless the particular implant has been demonstrated to be unaffected by the electromagnetic fields used for this imaging modality. Potential risks include injuries related to movement of ferromagnetic implants, excessive heating, induced electrical currents, the misinterpretation of an artifact as an abnormality, and temporary or permanent implant damage. To date, several neuromodulation systems have been tested using *ex vivo* techniques, resulting in FDA approved labeling to permit patients to undergo MRI. This presentation will provide an overview of MRI-related issues for neuromodulation systems and discuss current information pertaining to devices that have been tested, to date.

Learning Objectives
At the completion of this presentation, participants should be able to:
1. Provide an overview of MRI procedures and safety issues;
2. Describe comprehensive screening procedures to prepare patients with neuromodulation devices for MRI exams;
3. Present the latest information pertaining to MRI safety for patients with neuromodulation devices.

References
1. Shellock FG. *Reference Manual for Magnetic Resonance Safety, Implants and Devices: 2008 Edition,* Biomedical Research Publishing Group, Los Angeles, CA 2008
2. Rezai AR, et al. *Neurostimulator for deep brain stimulation: Ex vivo evaluation of MRI-related heating at* 1.*5-Tesla.* Journal of Magnetic Resonance Imaging. 15:241-250, 2002.

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3. Shellock FG. Begnaud J, et al. *VNS Therapy System: In vitro evaluation of MRI-related heating and function at 1.5- and 3-Tesla.* Neuromodulation, 9:204-213, 2006.
4. Henderson JM, Tkach J, Phillips M, et al. Permanent neurological deficit related to magnetic resonance imaging in a patient with implanted deep brain stimulation electrodes for Parkinson's disease: case report. Neurosurgery. 2005;57(5):E1063;
5. Rezai AR, Baker KB, Tkach JA, et al. Is magnetic resonance imaging safe for patients with neurostimulation systems used for deep brain stimulation? Neurosurgery. 200;57:1056-62.

0920 - 1000 Princesa Ballroom B-C (13)
Surgery for Obsessive-Compulsive Disorder – See Non CME Syllabus for Information
Bart Nuttin, MD, PhD

1030 -1110 Princesa Ballroom B-C (13)
Surgery For Depression
Ali Rezai, MD
Center for Neurological Restoration, Director
Cleveland Clinic
Cleveland, Ohio USA

1110 – 1200 Princesa Ballroom B-C (13)
The DBS of Pedunculopontine Nucleus in Parkinson's Disease
Paolo Mazzone MD, PhD
OU. Functional and Stereotactic Neurosurgery CTO
"A. Alesini " Hospital
Rome, Italy

Abstract
Background: Deep brain stimulation (DBS) is commonly applied to the treatment of movement disorders, and particularly Parkinson's Disease (PD), in human subject. The Peduncolopontine nucleus (PPN, Tg pd po, PPTgN), has recently become a target for DBS in PD; in particular, PPN-DBS seems effective in ameliorating postural abnormalities and gait.

Objective: To describe the pre-surgical planning, the surgical procedure and the outcome of the targeting of PPN in humans.

Methods: 12 patients, 8 with bilateral PPN implantation, 4 with unilateral lead, are considered. Two targeting strategies are described: a traditional, "indirect" method based on stereotactic ventriculography (12 leads implanted – 6 patients) with classical proportional determination and S&W overlapping of 2D slides; and a more recent "direct" method, based on a digital elaboration of stereotactic CT scan (8 leads implanted - 6 pt) on which is planned a 3D reconstruction of anatomical targets.

Results: All patient received implantation of the leads in the PPN, below the Ponto-Mesencephalic line. None developed major complications during or after the surgery; transient paresthesias were elicited at the start of DBS. The comparison between the 'indirect' and the 'direct' approaches suggest that the former has a high degree of approximation when brainstem structures are targeted.

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Discussion: The necessity to target the PPN made it necessary to develop a novel stereotactic approach to DBS. The classic, rigid, coordinates determination based on the anatomical definitions of brain atlases, utilizing the Ca–Cp plane must be re-considered in this surgery, since it can become potentially incorrect in target definition and, therefore, questionable. Moreover intraoperative IOMER is not helpful to define the borders of PPN; the post-operative recordings from contact leads (Blink-reflex, H – reflex) are more reliable and repetitive in the identification of PPN activity and represent a better link with clinical findings. In the future, the neuroimaging techniques will represent a new objective tool to identify the target area. From surgical point of view, in the future the use of microarrays or microprobes will potentially contribute to overcome these actual limitations.

References

1. Mazzone P. et al.: DBS in Movement Disorders: where are we going .Proceedings of 14th WSSFN, Rome, June 2005, Monduzzi Eds. , 2005.

2. Mazzone P, Lozano A, Stanzione P, Galati S, Scarnati E, Peppe A, Stefani A. Implantation of human pedunculopontine nucleus: a safe and clinically relevant target in Parkinson's disease. Neuroreport. 2005 Nov 28;16(17):1877-81.

3. Stefani A, Lozano AM, Peppe A, Stanzione P, Galati S, Tropepi D, Pierantozzi M, Brusa L, Scarnati E, Mazzone P. Bilateral deep brain stimulation of the pedunculopontine and subthalamic nuclei in severe Parkinson's disease. Brain. 2007 Jun;130(Pt 6):1596-607. Epub 2007 Jan 24.

4. Mazzone P, Insola A, Lozano A, Galati S, Scarnati E, Peppe A, Stanzione P, Stefani A. Peripeduncular and pedunculopontine nuclei: a dispute on a clinically relevant target. Neuroreport. 2007 Aug 27;18(13):1407-8.

Learning Objectives

At the completion of this presentation, participants should be able to:

1. Realize the rationale of PPN DBS;
2. Estimate the peculiarities of the surgical approach to PPN;
3. Appraise the clinical outcome of implanted patients;
4. Criticize the present literature data.

1300 – 1415 Princesa Ballroom B-C (13)
CME Luncheon Symposium - Intrathecal Therapy: Evolving Options and Ideas

Timothy R. Deer, MD, FIPP, DABPM
President and CEO, The Center for Pain Relief
Clinical Professor, West Virginia University
Charleston, West Virginia USA

Joshua P. Prager, MD, MS
Director, California Pain Medicine Center
Center for Rehabilitation of Pain Syndromes
David Geffen School of Medicine
University of California at Los Angeles
Los Angeles, California USA

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Lynn R. Webster, MD
Medical Director
Lifetree Clinical Research and Pain Clinic
Salt Lake City, Utah USA

Agenda

1300 PM	Opening Comments and Objectives	Timothy R. Deer, MD, FIPP, DABPM
1305 PM	Update on the 2007 Polyanalgesic Consensus Conference Treatment Algorithm	Timothy R. Deer, MD, FIPP, DABPM
1325 PM	Combination Intrathecal Therapy: Evaluating the Literature	Lynn R. Webster, MD
1345 PM	Update on Intrathecal Granulomas	Joshua P. Prager, MD, MS
1405 PM	Questions and Answers	Faculty
1415 PM	Closing Comments/Adjourn	

Abstract
Periodic reviews of new literature, clinical practices, and treatment options have prompted regular updates of the Polyanalgesic Consensus Conference (PACC) intrathecal (IT) treatment algorithm. Combination IT therapy has become more common as the number of agents used for IT therapy has increased. Consequently, the clinical implications of IT drug combinations need to be evaluated, as well as the chemical stability of the combined drugs. Earlier reports linked the development of catheter tip granulomas to the administration of IT opioids, but recent evidence suggests that most IT analgesics are associated with a risk for this rare but potentially devastating complication. In this symposium, the 2007 PACC IT treatment algorithm will be described, evidence for the use of combination IT therapy will be evaluated, recent reports of catheter tip granulomas will be discussed, and prevention, detection, and management strategies for IT granulomas will be described.

Learning Objectives

At the conclusion of this symposium, the participant should be able to
1. Describe the 2007 PACC IT treatment algorithm;
2. Evaluate recent evidence for the use of combination IT therapy;
3. Discuss new reports of IT granuloma formation and identify potential risk factors;
4. Describe methods for the prevention, detection, and management of IT granulomas.

1415 – 1715 Marquesa Ballroom I-II (16)
Deep Brain Stimulation
Ali Rezai, MD – Session Chair
Cleveland Clinic
Center for Neurological Restoration, Director
Cleveland, Ohio USA

1415 – 1540 Marquesa Ballroom lll-lV (16)
Intrathecal Polyanalgesia
Timothy R. Deer, MD, FIPP, DABPM – Session Chair
President and CEO, The Center for Pain Relief
Clinical Professor, West Virginia University
Charleston, West Virginia USA

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1415 - 1715 Atlantes
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1415 -1440 Marquesa Ballroom I-II (16)
Modeling the Effects of Neuromodulation at the Single Cell and Network Levels
Cameron McIntyre, PhD
Cleveland Clinic, Lerner College of Medicine
Department of Biomedical Engineering
Cleveland, Ohio USA

Abstract
Deep brain stimulation (DBS) is an effective clinical treatment for several medically refractory neurological disorders. However, the clinical successes of DBS are tempered by our limited understanding of the effects of the stimulation on the nervous system, and scientific definition of the therapeutic mechanisms of DBS remains elusive. In addition, it is presently unclear what electrode designs and stimulation parameters are optimal for maximum therapeutic benefit and minimal side effects. This presentation will describe our attempts to integrate neuroanatomical, neurophysiological, and electrical data to create a computational framework that enhances our understanding of the effects of DBS and provides a virtual testing ground for new stimulation paradigms.

Learning Objectives
At the conclusion of this symposium, the participant should be able to
1. Quantify the electric field generated by deep brain stimulation;
2. Characterize the neural activation that occurs as a direct result of applied electric fields;
3. Simulate the response of stimulation induced activity in large scale neural networks;
4. Identify techniques to experimentally validate detailed theoretical models of neuromodulation.

1415 – 1440 Marquesa Ballroom lll-lV (16)
Managing the Device: What do I do when a pump or catheter malfunctions?
Robert Levy, MD, PhD
Northwestern Medical Faculty Foundation, Inc.
Department of Neurological Surgery
Chicago, Illinois USA

1440 – 1500 Marquesa Ballroom I-II (16)
Cerebrospinal Stimulation Therapy for the Treatment of Vegetative State and Minimally Conscious State
Takamitsu Yamamoto MD, PhD
Division of Applied System Neuroscience
Department of Neurological Surgery
Nihon University School of Medicine
Tokyo, Japan

Abstract
The Multi-Society Task Force on PVS (1994) summarized the medical aspects of the vegetative state. They provided a statement that the VS is a clinical condition of complete unawareness of the self and the environment, accompanied by sleep-wake cycles, with either complete or partial preservation of hypothalamic and brainstem autonomic function. However, there are various grades of severity and various stages

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leading to various outcomes, even if the patient displays neurological signs identical to the VS.

We evaluated patients in the VS by an electrophysiological approach, and compared the results of the examination with the long-term prognosis. Twenty-one cases of a vegetative state (VS) caused by various kinds of brain damage were evaluated neurologically and electrophysiologically at 3 months after brain injury. These cases were treated by deep brain stimulation (DBS) therapy, and followed up for over 10 years. The mesencephalic reticular formation was selected as a target in 2 cases, and the thalamic centre median-parafascicular (CM-pf) complex was selected as a target in the other 19 cases.

Eight of the 21 patients emerged from the VS, and became able to obey verbal commands. In the 8 cases that emerged from the VS following DBS therapy, the Vth wave of the ABR and N20 of the SEP were recorded even with a prolonged latency; continuous EEG frequency analysis demonstrated a desynchronization pattern or slight desynchronization pattern; and the pain-related P250 was recorded with an amplitude of over 7 mV. However, they remained in a bedridden state except for 1 case. DBS therapy may be useful for allowing patients to emerge from the VS, if the candidates are selected according to appropriate neurophysiological criteria. A special neurorehabilitation system may be necessary for emergence from the bedridden state in the treatment of VS patients.

On the other hand, the definition of the minimally conscious state (MCS) is characterized by inconsistent but clearly discernible behavioral evidence of consciousness and can be distinguished from coma and the VS by documenting the presence of specific behavioral features that are not found in either of these latter conditions. DBS therapy and spinal cord stimulation (SCS) therapy can be a useful method in minimally conscious state (MCS) patients to achieve consistent discernible behavioral evidence of consciousness, and emergence from the bedridden state.

Learning Objectives
At the completion of this presentation, participants should be able to:
1. Distinguish between vegetative state (VS) and minimally conscious state (MCS);
2. Describe the electrophysiological evaluation method for the selection of candidate;
3. Restate the long-term follow-up results after deep brain stimulation and spinal cord stimulation;

1440 – 1500 Marquesa Ballroom lll-lV (16)
Managing the Infusion: Which drug should I use and when should I use It?
Timothy R. Deer, MD, FIPP, DABPM
President and CEO, The Center for Pain Relief
Clinical Professor, West Virginia University
Charleston, West Virginia USA

Abstract
Introduction: The use of intrathecal drug infusions has become a common practice in the treatment of moderate to severe pain syndromes. The devices were first used clinically over twenty years ago to treat patients with cancer related pain syndromes and spasticity, but in current times are more commonly used to treat patients with chronic non-cancer pain. With the treatment of patients with a prolonged life expectancy there

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is a challenge to maintain a reasonable outcome, patient satisfaction, and to maintain safety.

Initial Treatment: Once a chronic pain patient has been evaluated and selected for an intrathecal pump the physician must choose the drug to infuse. This process can be determined at the time of the pump trial, or may be modified at the placement of the permanent pump. The Food and Drug Administration has approved Morphine and Ziconotide for the initial treatment of pain by the intrathecal route. A consensus panel of experts evaluating the world literature also concluded that hydromorphone is a reasonable choice for first line therapy. The decision to change drugs is based on the inability to produce good efficacy or because of side effects. This is a critical time in the care of the patient since the choices of the physician will determine the success of the device. Since these devices are often placed as a last resort, treatment failure is disturbing.

Algorithmic Treatment: The evidence for making changes in the infusion should be based on patient safety, evidence based support of the drug, and clinical experience in similar patients. The off label use of a drug is sometimes needed, but should be based on these criteria and also based on what other practitioners in your field are doing clinically. The agents chosen are based on the character of the pain and the reason for the change. Bupivacaine and Clonidine are sometimes added to opioids to treat neuropathic pain conditions. The use of Fentanyl is chosen when other opioids produce relief, but cause unacceptable side effects. Ziconotide can be chosen as a first line agent or as an adjuvant when opioids are not sufficient. Polyanalgesic infusions are sometimes used, and should be based on acceptable toxicity, compatibility and stability. This is often done to maintain a reasonable drug concentration of the primary opioid.

End of Life Care: In some patients the ability to manage pain is very difficult, and commonly used drugs do not give acceptable outcomes. In end of life care some have recommended considering agents that are not indicated in other patients because of the risk of neurotoxicity. Agents in this group include methadone, tetracaine, midazolam, droperidol, and ondansetron. The use of these drugs should be approached with caution.

References

Deer T, Krames E, Hassenbusch S, Burton A, Caraway D, DuPen S, Eisenach J, Erdek M, Grigsby E, Kim P, Levy R, McDowell G, Mekhail N, Panchal S, Prager J, Rauck R, Saulino M, Sitzman T, Staats P, Stanton-Hicks M, Stearns L, Willis D, Witt W, Follett K, Huntoon M, Liem L, Rathmell J, Wallace M, Buscher E, Cousins M, Ver Donck A. Polyanalgesic Consensus Conference 2007: Recommendations for the Management of Pain by Intrathecal (Intraspinal) Drug Delivery: Report of an Interdisciplinary Expert Panel. Neuromodulation: Technology at the Neural Interface. Vol 10,(4). October 2007.

Learning Objectives

At the completion of this presentation, participants should be able to:

1. List the first line therapies for use in an intrathecal pump;
2. Define the proper algorithms for use in patients who do not respond to initial therapy;
3. Explain the proper use of drugs in the patient with end of life disease.

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1500 - 1520 Marquesa Ballroom I-II (16)
Deep Brain Stimulation for Tourette's Syndrome
Osvaldo Vilela Filho, MD, PhD
Stereotactic and Functional Neurosurgery Service, Head of Service
Hospital das Clinicas, Medical School, Federal University of Goias2
nstituto de Neurologia de Goiania
Goiania, Goias, Brazil

Abstract
Although frequently self-limited, when persistent, Tourette syndrome (TS) presents a high intractability rate, 1/3 of the patients remaining disabled throughout their adult lives in spite of adequate conservative treatment. In such cases surgery may be contemplated. Ablative surgery, using a variety of both motor and/or limbic targets, started in 1962, and in a review of 56 reported in the literature from 1962 and 1994, significant and moderate improvement was achieved in, respectively, 49% and 12% of the patients, at the cost of a neurological morbidity of 28% (Vilela Filho et al, 1998a). Vandewalle et al, 1999, were the first to perform DBS for the treatment of TS (one patient). The target used was the same as described by Hassler and Dieckmann in 1970 to place lesions to treat the same condition: bilateral CM/Pf. The good results reported (70-90% of tics reduction) have been replicated by others. Bilateral GPi-DBS, assessed by other groups since 2002, also looks like a promising target, while bilateral stimulation of the anterior capsule, evaluated by one group, provided only modest results.

Vilela Filho and Sousa (1996, 1998b), performing a wide review of the literature, pioneerly hypothesized that TS is the clinical expression of the hyperactivity of the globus pallidus externus (GPe) and prefrontal area, and probably, also, of other cortical regions, such as the motor and Broca's areas. Based on this hypothesis and considering the inexistence of a good animal model for this disorder and that deep brain stimulation of a nuclear structure produces its functional inhibition, the authors, approved by the Brazilian Ministry of Health Ethics Committee in 2001, started a prospective double blind controlled study to evaluate the effectiveness of bilateral GPe-DBS in patients harboring refractory TS. Due to its connections with the sensorymotor territory of STN, the central part of GPe was chosen as the primary target.

So far, three patients (all male, ages 18, 18 and 35) have been operated on. Diagnosis was established based on TS Study Group criteria and DSM IV. Surgery was considered only in patients considered refractory to conservative management (optimized pharmacotherapy and psycho- and behavioral therapy failed to improve the symptoms and quality of life and/or produced unacceptable side-effects). Preoperative assessment included MRI, SPECT or PET, neuropsychological, neurological and psychiatric evaluation (including validated scales for tics - YGTSS and obsessive-compulsive symptoms -YBOCS), and intracarotid propofol injection test - ICPIT (a test that we designed to determine if tics could be reduced by unilateral hemispheric deactivation). Target coordinates were obtained from IR MRI coronal and axial slices. Physiological mapping was performed through macroelecrode stimulation. Quadripolar DBS electrodes were implanted bilaterally, and connected to the internal pulse generator (s) in the same procedure. Pre- and postoperative video-recording was performed. To determine the clinical response to DBS, YGTSS and YBOCS scores obtained preoperatively were compared to those obtained postoperatively. In the postoperative period, evaluation with the stimulation on and off was performed in a double blind fashion (patient and rater, one of the investigators, were unaware of this fact); the scores so obtained were also compared.

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Preoperative MRI was normal in all patients and the SPECT (1 patient) and FDG-PET-scan (2 patients) demonstrated hyperactivity in the right prefrontal area and left motor area in the 3 patients, and also probably in GPe in 2 of them. ICPIT showed tics reduction after left side injection in 2 patients, and after right side injection in 1. Postoperative MRI confirmed adequate electrode placement in all. The follow-up periods were the following: 42 months (patient # 1), 7 months (patient # 2) and 1 month (patient number 3). Patient # 1, 2 and 3 were improved, according to the YGTSS and YBOCS, by, respectively: 82/84%, 74/29%, and 76/61%.

The results here reported, as well as the abnormalities seen on PET-scan, give further support to Vilela Filho & Sousa hypothesis, and are compared with the results obtained from stimulation of other targets currently under evaluation (CM/Pf and GPi).

References

Vandewalle V, van der Linden C, Groenewegen HJ, et al: Stereotactic treatment of Gilles de la Tourette syndrome by high frequency stimulation of thalamus. Lancet 1999; 353:724 (Letter).

Hassler R, Dieckmann G. Traitement stereotaxique des tics et cris inarticule our coprolaliques consideres comme phenomene d'obsession motrice au cours dela maladie de Gilles de la Tourette. Rev Neurol 1970; 123: 89-100

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Vilela Filho O; Ragaz\o PC, Silva DJ, Sousa JT, Oliveira PM, Ribeiro TMC. Bilateral Globus Pallidus Externus Deep Brain Stimulation (GPe-DBS) for the Treatment of Tourette Syndrome: an Ongoing Prospective Controlled Study (Abstr.). Stereotact Funct Neurosurg 2007; 85: 42-43.

Learning Objectives

At the conclusion of this activity, participants should be able to:

1. Comprehend the changes in the neurotransmitter's environment of patients with Tourette syndrome;
2. Interpret the findings obtained from functional neuroimaging studies in patients with Tourette syndrome and their importance;
3. Compare the results of the different targets used for stimulation in patients with Tourette syndrome;
4. Comprehend the rationale for the use of GPe as the target of choice.

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1500 – 1520 Marquesa Ballroom lll-lV (16)
Managing the Future: What can I expect from the future of intrathecal therapy?
Samer N. Narouze, MD, MS, DABPM
Program Director, Pain Medicine Fellowship
Pain Management Department, Division of Anesthesiology
Cleveland Clinic Foundation
Cleveland, Ohio USA

1520 – 1540 Marquesa Ballroom I-II (16)
DBS for Hypertension
Alexander L. Green FRCS (SN), MD, BSc
University of Oxford
John Radcliffe Hospital
Oxford, UK

Abstract
The 'periaqueductal gray' matter (PAG) is a brain region that is chronically stimulated in patients with severe, intractable neuropathic pain. However, in animals it has been known for some time that the PAG controls cardiovascular responses to stressful situations. We started by looking at the acute effects of PAG stimulation on blood pressure and pulse rate and found that PAG stimulation can indeed increase or decrease blood pressure, depending on whether the electrode is ventrally or dorsally located within the PAG (Green A.L. 2005). Furthermore, power spectral analysis of the blood pressure suggests that the changes are mediated by the sympathetic nervous system. A study on a hypertensive patient revealed that stimulation could reduce blood pressure to within the normal range (Green et al 2007).

If we can control hypertension, the possibility exists that we may be able to control 'orthostatic hypotension' – a debilitating condition that leads to a fall in blood pressure on standing. We therefore investigated the effects of PAG stimulation on the postural blood pressure response in eleven patients. This showed that, indeed, the postural effects on blood pressure can be modified (Green, Wang et al. 2006a). Similar to the direct blood pressure changes, these effects were also related to alterations in the sympathetic nervous system. However, in addition, the baroreceptor sensitivity was calculated in this study, revealing that PAG stimulation increases baroreceptor sensitivity and lessens the reduction of baroreceptor sensitivity on standing.

These two major findings i.e. that hypertension or orthostatic hypotension can potentially be altered with brain stimulation have led to our current studies looking at the long-term effects of stimulation on cardiovascular parameters, as well as the design of a device that may, after future development, be used to control a patient's blood pressure on a chronic basis.

As we had a cohort of patients with both pain scores and cardiovascular parameters, we have looked at the relationship between the two. The results show that those patients with the greatest reduction in blood pressure (in the acute phase of stimulation at least) also have the greatest analgesia as a result of stimulation. Indeed, the relationship between the two was a significant linear correlation ($p<0.01$)(Green, Wang et al. 2006b). This has two implications. Firstly, it provides a clue as to the mechanism of deep brain stimulation for neuropathic pain. Secondly, it provides direct evidence that William James (in 1884) was (at least) partly correct in stating that pain is due to alterations in blood pressure. Whether the pain sensations are directly linked to blood pressure or

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changes in sympathetic activity, or whether changes in these two are simply a corollary of alterations in PAG activity remain to be investigated.

References

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2. Green, A.L., Wang, S., Owen, S.L., Xie, K., Bittar, R.G., Stein, J.F., Paterson, D.J., and Aziz, T.Z., Stimulating the human midbrain to reveal the link between pain and blood pressure, Pain, 124 (2006b) 349-59.

3. Green A.L., Wang S, Owen S.L.F., Xie K., Liu X., Paterson DJ, Stein J, Bain P, Aziz T. Deep Brain Stimulation Can Regulate Arterial Blood Pressure in Awake Humans, Neuroreport, 16 (2005) 1741-5.

4. Green A.L, Wang S, Bittar R.G, Owen SLF, Paterson DJ, Stein JF, Bain PG, Shlugman D, Aziz TZ. Deep Brain Stimulation: A New Treatment for Hypertension? J Clin Neurosci, 14(2007) 592-5

Learning Objectives

At the completion of this presentation, participants should be able to:

1. Describe how the periaqueductal gray area can influence blood pressure in the animal;
2. Assess cardiovascular effects of PAG stimulation in man;
3. Assess effects of PAG stimulation on the postural response of blood pressure;
4. Determine the potential for further therapy.

1520 – 1540 Marquesa Ballroom lll-lV (16)
Question and Answer

1540 – 1600 Marquesa Ballroom I-II (16)
Deep Brain Stimulation for Refractory Craniocervical Dystonia: One Year Follow-Up Result

Jin Woo Chang, MD, PhD
Department of Neurosurgery
Yonsei University College of Medicine
Seoul, Korea

Abstract

As pallidal surgery showed good effect in levodopa-induced dystonic dyskinesia and "off" period dystonic symptoms in Parkinson's disease (PD), pallidum has become the target of dystonia. I have experienced 22 patients of severe medically intractable dystonia treated by deep brain stimulation (DBS) since February 2002. Among those, 7 patients had severe refractory craniocervical dystonia with blepahrospasm (Meige's syndrome) and 6 patients could follow-up more than one year after pallidal deep brain stimulation (DBS). I will report and discuss about the role of DBS for Meige's syndrome.

All of the patients suffered for several years from medically refractory Meige`s syndrome. Mild involuntary contraction of their lower face was the first symptom, and then spasm of tongue during speeking was followed. At last, blepharospasm & craniocervical dystonia interfered with their ability to do her housekeeping and his job.

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DBS electrodes were implanted in posteroventral lateral globus pallidus internus (GPi) bilaterally. Microelectrode recordings were taken to localize GPi electrophysiologically. Intraoperative microstimulation of both GPi resulted in reproducible resolution of blepharospasm and craniofacial dystonia. Implantable pulse generator(IPG) was implanted in subclavicular subcutaneous area.

Our cases of bilateral pallidal DBS in patient with Meige`s syndrome showed remarkable improvements in one year follow-up period. We will show the detailed data regarding the improvement of symptoms of patients.

Learning Objectives
At the completion of this presentation, participants should be able to:
1. State the diagnosis of craniocervical dystonia;
2. Explain the DBS procedure for dystonia;
3. Describe the progress of improvement of DBS for craniocervical dystonia.

1530 - 1650 Marquesa Ballroom I-II (16)
Neuromodulation for Anorexia Nervosa
Bomin Sun, MD
Shanghai Jiao Tong University
Ruijin Hospital
Shanghai, China

Abstract
Objective: To study the effect and complications of bilateral capsulotomy and nucleus accumbens (NAc) stimulation in refractory anorexia nervosa.

Methods: Stereotactic surgery was performed on 20 patients with refractory anorexia nervosa who underwent ineffective psychotherapy and pharmaceutical therapy. 3 patients received bilateral NAc deep brain stimulations and 5 patients received bilateral anterior capsulotomy. 12 patients received right capsultomy combined with left NAc stimulation. The targets of anterior internal capsule and nucleus accumbens were identified directly under high resolution magnetic resonance imaging. Radiothermal lesions were made at 80°C for 60 seconds. Deep brain stimulation electrodes (DBS, model 3387) were implanted similar to surgical procedures in Parkinson's disease. We also took pre-op and post-op F^{18} positron emission tomography (PET) scans in all patients.

Results: All patients were followed up from 2 to 26 months (mean 10.4 months). All 5 cases with bilateral capsultomy demonstrated an immediate improvement: patients recovered normal eating and concurrent psychiatric symptoms had significant improvement as well. Their body weight gained from 8-20 kg in 2 months after surgery. All patients with bilateral DBS had significant improvement in obsessive-compulsive and anxiety symptoms, but little improvement in eating behavior or body weight gain. Patients who underwent unilateral capsulotomy combined with unilateral NAc DBS showed significant improvement in both eating behavior and psychiatric symptoms.

Temporary side effect such as urinary incontinence, memory loss and confusion were seen in bilateral capsulotomy patients. These side effects usually recovered in one week. No other side effects were observed in other patients.

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In F^{18} PET studies, all patients demonstrated a significant increase of metabolic levels in bilateral orbital frontal cortex, cingulum as well as caudate pre-operatively. Metabolic

levels in these areas dropped after surgery in both DBS and lesioning patients, and this drop was more significant in lesion side than stimulation side.

Conclusion: Lesioning of anterior internal capsule and/or stimulation of NAc are very effective for medically refractory anorexia nervosa. The complications of surgeries are mild. The surgical procedures are very promising and should serve as an alternative therapy in advanced anorexia nervosa.

Learning Objectives

At the completion of this presentation, participants should be able to:

1. Contrast clinical outcomes resulting from bilateral capsultomy, bilateral DBS, and unilateral capsulotomy combined with unilateral NAc DBS;
2. List side effects and complications of these interventions.

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0800 – 1200 Princesa Ballroom B-C (13)
Plenary Session: Pain Day
Joshua P. Prager, MD, MS – Session Chair
Director, California Pain Medicine Center
Center for Rehabilitation of Pain Syndromes
David Geffen School of Medicine
University of California at Los Angeles
Los Angeles, California USA

0800 – 0840 Princesa Ballroom B-C (13)
Evidence Based Neuromodulation
John D. Loeser, MD
Department of Neurological Surgery
University of Washington
Seattle, Washington USA

Abstract
Whether we like it or not, evidence-based medicine (EBM) is rapidly changing the way that interventions will be recommended and funded. Those who perform neuromodulation procedures need to be aware of what our evidence base currently is and how we can move from the trough of this wave to its crest. Those who utilize these strategies must contribute to the acquisition of knowledge about their outcomes, including benefits, risks and costs. We cannot just claim that EBM does not apply to what we do.

Learning Objectives
At the conclusion of this presentation, participants should be able to:
1. Analyze evidence for neuromodulation for pain relief;
2. Discuss issues in validating efficacy for neuromodulation for pain;
3. Propose strategies for improving studies on neuromodulation for pain.

0840 – 0920 Princesa Ballroom B-C (13)
Cellular/Physiological Mechanisms of Stimulation
Robert D. Foreman, PhD, FAHA
University of Oklahoma Health Sciences Center, College of Medicine
Department of Physiology
Oklahoma City, Oklahoma USA

Abstract
The purpose of this presentation is to discuss the physiological mechanisms underlying the effects of neuromodulation in normal animals as well as animal models exhibiting different pathological conditions. These models will be used to discuss some of the mechanisms that are activated during spinal cord stimulation to provide pain relief and improve organ function. Knowledge of physiological mechanisms is an essential requirement of the medical profession as it endeavors to move towards evidence-based therapies. The mechanisms of neuromodulation differ between the pathologies treated and the location along the neuro-axis where the stimulus is applied. The presentation will discuss how SCS applied at various levels of the neuro-axis induces changes in different target organs mediated via stimulation-induced changes in local autonomic activity, dorsal root reflexes, spinal neuronal processing, or on viscero-somatic reflexes. The detailed exploration of physiological mechanisms has also proven necessary for the

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further development of the techniques used in neuromodulation. We firmly believe that SCS at present is an under-used treatment modality because the physiological mechanisms producing the beneficial effects have not been elucidated. The results of these studies will lead to improvement and expansion of future neuromodulation therapies that will be of benefit to patients.

Learning Objectives
At the conclusion of this presentation, participants should be able to:
1. Examine physiological mechanisms that are activated by neuromodulation;
2. Compare and contrast the effects of neuromodulation at different levels of the spinal cord;
3. Demonstrate that neuromodulation improves organ function.

0920 – 1000 Princesa Ballroom B-C (13)
Mechanisms of Action Of Deep Brain Stimulation
Warren M. Grill, PhD
Department of Biomedical Engineering
Duke University
Durham, North Carolina USA

Abstract
Deep brain stimulation (DBS), has evolved from a highly experimental technique to an established therapy for the treatment of movement disorders including dystonia, essential tremor, and Parkinson's disease. While the clinical benefits of DBS are well documented, fundamental questions remain about the mechanisms of action. In particular, it is unclear how high-frequency stimulation results in outcomes similar to those from lesions of target structures in the thalamus or basal ganglia. The effects of extracellular stimulation on the pattern of activity in CNS neurons will be reviewed and used to motivate of a hypothesis that DBS acts by regularizing the activity in affected neurons. Two studies of the effect of stimulation frequency and stimulation regularity on tremor and pattern of neuronal activity will be presented. The correlation between the changes in tremor and the changes in neuronal firing supports the hypothesis that regularization of neuronal firing pattern during DBS is one of the mechanisms underlying tremor suppression.

Learning Objectives
At the conclusion of this presentation, participants should be able to:
1. State the dual effects of DBS on neurons;
2. Explain the effect of stimulation frequency on the pattern of neuronal activity;
3. Describe the effects of stimulation pattern on the efficacy of DBS.

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Acknowledgements
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1000 – 1015
Break

1015 – 1045 Princesa Ballroom B-C (13)
NANS General Assembly

1045 – 1125 Princesa Ballroom B-C (13)
Mechanisms of Headache
Peter J. Goadsby, MD, PhD
University of California, San Francisco
Department of Neurology
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Institute of Neurology, Queen Square
London, UK

Abstract
Primary headache disorders, headache syndromes without apparent external cause, are among the most common drivers to attendance in primary care and certainly in neurology. Migraine alone affects more than 25 million Americans (1) and costs some $20 billion per year in the US alone (2). The last decade has seen considerable advances in our understanding of the pathophysiology of primary headache disorders alongside some impressive improvements in treatment (3).

Key to understanding many of the presentations in primary headache disorders is the anatomical/physiological basis of the pain. The largest part of the pain-producing structures within the head, the perivascular dura mater, are supplied by branches of the trigeminal nerve, particularly the first or ophthalmic division. Its projection to the trigeminal nucleus caudalis and extension to the dorsal horns at C1/C2 overlaps with the night cervical input that arises largely from the C2 root and innervates the infratentorial and posterior cranial structures (4). This collection of neurons, the trigeminocervical complex (TCC), is the shared pathway for pain expression in the primary headaches. Functional imaging data (5), taken with the very clear clinical syndromes set out in the International Classification of Headache Disorders (6) suggest that the headache syndromes are best differentiated as disorders of brain mechanisms involved in the gating and modulation of sensory input, such as that from the TCC. A recent development in this area has been the extension of these concepts to neuromodulatory approaches to the management of medically intractable primary headache disorders (7, 8).

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Learning Objectives

At the conclusion of this presentation, participants should be able to:

1. Discuss developments in the understanding of the pathophysiology of primary headache disorders.

1125 – 1205 Princesa Ballroom B-C (13)

Model Predictions and Their Empirical Validation: What have we learned from modeling spinal cord stimulation?

Jan Holsheimer, PhD
Institute for Biomedical Technology, University of Twente
Enschede, The Netherlands

Abstract

An overview of the main results of modeling spinal cord stimulation (SCS) over the last 20 years is presented. To validate the predictions based on these theoretical studies they are compared to the outcome of clinical studies.

Generally, a complete coverage of the pain area with paresthesia cannot be achieved because the therapeutic stimulus magnitude is limited by the discomfort threshold (DT), which is related to stimulation of proprioceptive dorsal root (DR) fibers [1]. It is shown that the main parameters affecting paresthesia coverage are (i) the cathode-anode configuration, (ii) the center distance between the electrodes and (iii) the distance between the lead(s) in the dorsal epidural space and the spinal cord. It is predicted that dorsal column (DC) and DR nerve fibers respond differently to changes of these parameters and that paresthesia coverage is largest in bipolar and tripolar ("guarded cathode") stimulation with a small center distance of the electrodes (~4 mm) and a small lead-to-spinal cord distance (2-3 mm) [2,3]. When DC fibers have a higher threshold than DR fibers the latter set the perception threshold (PT), whereas DT exceeds PT by about

40%. When DC fibers have the lower threshold these fibers set PT, while DT exceeds PT by >40% (up to >100%) [1].

Taking into account the cephalo-caudal variation of (i) the lead-to-spinal cord distance and (ii) the latero-medial displacement of DC fibers, it is hypothesised why stimulation of the low-back is restricted to a "sweet spot" or fails. It is also predicted that the main favorable effect of dual-lead stimulation is an increase of the volume of the dorsal epidural space, displacing the dura mater anteriorly and reducing the lead-to-spinal cord distance resulting in an increased paresthesia coverage [4,5].

Until recently, SCS techniques to improve the overlap of pain with paresthesia were actually maximizing the area of paresthesia, because the available single channel pulse generators do not allow controlled paresthesia displacement. We introduced the principle of transverse tripolar (guarded cathode) SCS with two pulse generators giving simultaneous pulses with independently controlled amplitude. This TTL system allows smooth medio-lateral field steering in the DCs, smoothly shifting paresthesia to cover the pain [6,7].

It is demonstrated that most characteristics of SCS as predicted by modeling are in accordance with clinical data, demonstrating that the UT-SCS computer model is an appropriate tool in neuronal stimulation research.

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Learning Objectives

At the conclusion of this presentation, participants should be able to:

1. Describe what the computer model calculates;
2. Identify the geometric parameters affecting paresthesia coverage most, and describe the conditions favoring a large coverage;
3. Indicate which anatomical variables determine the presence or absence of a "sweet spot" in SCS of the low-back;
4. Explain why dual-lead stimulation may favor a large paresthesia coverage;
5. Clarify why paresthesia can only be steered in a controlled way to the pain when at least two pulse generators, giving simultaneous pulses with independently controlled amplitude, are used.

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1200 – 1300 Break

1300 – 1415 Ballroom B-C (13)
Commercial Luncheon Symposium - see Non-CME Syllabus for details

1415 – 1515 Marquesa Ballroom I-II (16)
Deep Brain Stimulation and Motor Cortex Stimulation
Ali Rezai, MD – Session Chair
Cleveland Clinic
Center for Neurological Restoration, Director
Cleveland, Ohio USA

1415 – 1520 Marquesa Ballroom lll-lV (16)
Neuromodulation for Eyesight and Hearing
Paul Meadows, PhD - Session Chair
Boston Scientific
Valencia, California USA

1415 – 1715 Atlantes
Commercial Symposium – see Non-CME Syllabus for information

1415 – 1440 Marquesa Ballroom I-II (16)
Treatment of Primary Camptocormia (dystonic bent spine or bent neck) by Electrical Stimulation of the Globus Pallidus Internus: Report of 3 Cases
Damianos E. Sakas, MD
University of Athens
Evangelismos Hospital
Department of Neurosurgery
Athens, Greece

Abstract
Introduction: Bilateral deep brain stimulation (DBS) of the globus pallidus internus (GPi) has increasingly been accepted as a reliable and effective treatment for dystonia.

Material-Methods: We report on three cases of drug-resistant primary camptocormia, i.e. dystonic bent spine or neck who were treated successfully by DBS of the GPi. The first patient, a female 26 years old, suffered for 3 years from so severe camptocormia that she became unable to walk and was confined in bed or wheel-chair. The second patient, a male 21 years old, suffered for 6 months from of less severe camptocormia; he could walk only for short distances with a very bent spine, the arms in a parallel position to the legs, and the hands almost approaching the floor to potentially support him and prevent his fall down to the ground. The third patient, a 49-year-old female, presented with a 6-year history of a 90^{o} head-drop, and inability to raise her head more than 30^{o} at any time (camptocephalia). All patients received chronic bilateral electrical stimulation of the posterolateroventral nucleus of the GPi. The optimal clinical result obtained when the stimulation settings were: voltage 2.2, 1.8, and 1.5V (respectively), pulse width 90_s, and frequency 130Hz.

Results: It is remarkable that all patients experienced marked clinical improvement within a postoperative period ranging from 5 days to 6 weeks. After 18, 16, and 11

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months of follow-up, respectively, all patients are entirely free of symptoms and have returned to a normal life with a full range of daily activities.

Conclusions: Bilateral DBS of the GPi may prove an effective treatment in medically refractory cases of primary axial dystonia which present with a bent spine. The reported favourable outcome of our patients suggests that a specific oscillatory activity in a somatotopically distinct GPi cluster may have been necessary for the adoption and maintenance of the erect posture by humans.

Learning Objectives
1. At the conclusion of this presentation, participants should be able to:
2. Review the applications of deep brain stimulation;
3. Describe new treatment options for medically-refractory primary axial dystonia.

1415 – 1440 Marquesa Ballroom III-IV (16)
Sensory Prosthetics for Hearing and Vision: Past, Present and Future
Robert J. Greenberg, MD, PhD
Second Sight Medical Products, Inc.
Sylmar, California USA

Abstract
In 1755 LeRoy discovered that an electric charge delivered to the blind eye produced a sensation of light. Ever since, man has pondered the possibility of making the blind see. However, it wasn't until the age of modern electronics that building such a device became possible. In the 1960's, Dr. Brindley in England elicited sensations of light in blind subjects by electrically stimulating their visual cortex (the back side of their brain). In the 1970's, Dr. Dobelle in the U.S. repeated these experiments with some success. However, the resolution achieved by these early devices was very poor. At best, these patients could read Braille by the flashing lights (phosphenes).

By the time the visual image has reached the brain, a significant amount of processing has already occurred - making fine resolution difficult to achieve. Another problem with this approach was that the surgery was very invasive and dangerous for these volunteer patients. In the 1990s at Johns Hopkins, we discovered that there is a subpopulation of blindness (outer retinal degenerations such as retinitis pigmentosa) in which a majority of the retina and visual system is intact, allowing stimulation more peripherally - at the retina.

By electrically stimulating the retinas of over a dozen of these patients in the operating room, we were able to achieve formed vision. Stimulating the retina has the potential to provide a much higher resolution device than stimulating the visual cortex and there are now half a dozen groups around the world pursuing this line of research. In the Los Angeles area in 1998, we formed a company called Second Sight, which has embarked on creating the first artificial retina - a long-term implantable system which will allow the blind to see.

Chronic implants of a first generation device were implanted in six patients from 2002 – 2004 at USC. A second generation device is now beginning international multi-center clinical trials.

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At the conclusion of this presentation, participants should be able to:
1. Describe which cells are damaged in retinitis pigmentosa;
2. Explain the advantage of retinal stimulation over cortical stimulation;
3. Describe the outcome of the Argus™ I trials.

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Acknowledgements

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1440 – 1500 Marquesa Ballroom I-II (16)
Deep Brain Stimulation for Pain

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Stanford, California, USA

Abstract

Deep brain stimulation (DBS) has been used to treat painful conditions since the 1950's. Advancements in both surgical targeting and knowledge of underlying brain circuitry have combined to improve the efficacy of DBS for pain. Although classified as an "experimental" procedure by the FDA, DBS may nonetheless offer some benefit for patients in whom there are no other treatment options. The history, indications, targets, and outcomes of DBS for pain will be reviewed.

Learning Objectives

At the completion of this presentation, participants should be able to:
1. Review the history of pain treatment using DBS;
2. Describe standard targets for DBS in the treatment of pain;
3. List painful conditions for which DBS is indicated;
4. Discuss outcomes of DBS for pain.

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1440 – 1500 Marquesa Ballroom lll-lV (16)
Advances in Processing Strategies for Cochlear Implants
John K. Niparko, MD
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Department of Otology/Neurotology - Division Director
Baltimore, Maryland USA

Abstract
The cochlear implant is best characterized as a device that provides access to voiced, musical and environmental sound. The device provides informational cues from the surroundings and from others that may escape visual detection. As the developmental effects of a profound hearing loss are multiple, cochlear implants have been applied to ever younger children in an attempt to mitigate delays in developmental learning, with oral language development recognized as the outcome of primary interest. In adults with acquired deafness, the reintroduction of sound produces impressive improvements in both sensitivity to sound and speech recognition. Through improved rates of stimulation, auditory stations within the brain appear capable of processing information from the implant to enable speech comprehension and oral language development.

Multichannel implants have replaced original single channel designs. Because they provide spectral information in addition to temporal and intensity cues, multichannel devices enable larger percentages of recipients to recognize the spoken word without visual cues. Testing under conditions of auditory (implant)-only input reveals significant open-set speech understanding capability (without visual cues) in more than 75% of patients after 3 years of device use.

Candidates for a cochlear implant are those identified as failing to achieve material benefit from the use of powerful hearing aids. The benefit provided by implants may vary with a number of conditions including: hearing history, age of deafness onset, age at implantation, etiology of deafness, linguistic abilities, and the presence of a motivated system of support of oral language development. A patient's health and environmental circumstances should be given individual consideration in judging candidacy for a cochlear implant. For children, planning rehabilitative and education services after surgery and activation of the device are critical considerations.

For more than two decades, implantable devices have been applied to deaf children as an increasingly large proportion of all cochlear implants placed. Now, more than half of all newly implanted devices are placed in children, and most of these in children under 5 years of age. Auditory thresholds of cochlear-implanted children allow access to auditory information beyond that available to deaf children who routinely use conventional amplification (hearing aids), offering a critical substrate for developmental learning.
One of the most important advances in the field of cochlear implantation relates to the improved fidelity with which sound is represented in the electrical code transmitted by the implant. With faster rates of stimulation has come greater access to pitch as well as timing cues contained in sound stimuli. Access to pitch appears to translate into improved voicing and articulation and, more recently, greater enjoyment of music.
The evolution of the cochlear implant is monumental for several reasons. The cochlear implant represents one of many innovative technologies that enable the rapid transfer of

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processed information. A unique feature of implant technology, however, is that it represents an alliance of strategies that process information via both manufactured and natural, neural circuits. To the extent that a cochlear implant can encode the sounds of speech with precision, the device can provide impressive opportunities for developmental learning as well as access to sound and spoken communication.

Learning Objectives
At the conclusion of this presentation, participants should be able to:
1. Express an understanding of cochlear implantation procedures;
2. Describe factors that impact electrical parameters of cochlear implantation procedures;
3. List options for cochlear implant programming.

1500 – 1520 Marquesa Ballroom I-II (16)
Neurostimulation for Learning Enhancement
Emad Eskandar, MD
Department of Neurosurgery
Massachusetts General Hospital
Harvard Medical School
Boston, Massachusetts USA

Abstract
The nuclei comprising the anterior striatum play a critical role in learning and motivation. Derangements of these nuclei are implicated in a broad range of diseases including depression, drug addiction, and learning disorders. Our hypothesis is that there are two streams of information processing in the anterior striatum, dorsal and ventral, that perform complementary but different roles. Specifically, we hypothesize that the dorsal stream, which includes the caudate (Cd), is involved in the executive aspects of associative learning, whereas the ventral stream, which includes the nucleus accumbens (NAc), is involved in providing motivation for the performance of learned behaviors.

Recent studies in our lab have demonstrated that intermittent electrical stimulation of the caudate, a nucleus in the basal ganglia, can significantly enhance the rate of visual-motor learning in primates. In addition, we have more recent data suggesting that the effects of stimulation are mediated by physically enhancing dopamine release. In essence, stimulation appears to function in a manner analogous to spontaneous learning, but in an amplified fashion that is under experimental control. This challenges the conventional view that learning is a complex process that is not amenable to direct modification. Moreover, it is commonly held that the learning rate of different animals or humans is relatively fixed. However, our data suggest that is possible to enhance learning beyond baseline rates, suggesting that there is in fact considerable room for improvement. In other words, even though primates or humans may have a natural rate of learning new associations, they underlying circuitry maybe able to learn at much higher rates.

This work suggests that the circuitry underlying associative learning can be directly and specifically enhanced, greatly speeding the process of recovery following brain injury.

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This idea has tremendous significance for treating or rehabilitating patients with a broad spectrum of brain disorders such as stroke, traumatic brain injury, and autism.

Learning Objectives

At the conclusion of this presentation, participants should be able to:
1. Describe the role of the basal ganglia in learning
2. Describe role of dopamine in learning
3. Describe the role of deep brain stimulation in modulating learning

1500 – 1520 Marquesa Ballroom III-IV (16)
Question and Answer

1520 – 1540 Marquesa Ballroom I-II (16)
Motor Cortex Stimulation for Pain
Jean-Paul Nguyen MD
Neurochirurgien
Professeur des Universités
Hôpital Henri Mondor
Créteil Cedex, France

The following individuals contributed significantly to this presentation.
S. Keravel - Service de neurochirurgie, Hôpital Henri Mondor, Créteil 94000, France.
J.P. Lefaucheur - Département des explorations fonctionnelles, Hôpital Henri Mondor.
S. Raoul - Service de neurochirurgie, Hôpital Laennec, Nantes 44000, France.
V. Roualdes. - Service de neurochirurgie, Hôpital Laennec, Nantes 44000, France.
Y. Péréon - Département des explorations fonctionnelles, Hôpital Laennec.

Abstract

Chronic motor cortex stimulation is a rapidly developing treatment modality, indicated for the treatment of chronic neuropathic pain refractory to analgesic medications. The indications essentially concern cases that cannot be treated by spinal cord stimulation: central pain and neuropathic facial pain. The mechanism of action is starting to be more clearly elucidated. PET studies have shown that the main mechanism of motor cortex stimulation is activation of pathways descending to the thalamus, brain stem and spinal cord which play a role in inhibition of pain messages. Activation of these controls theoretically requires at least partial integrity of sensory pathways and the pyramidal tract. These studies also showed that motor cortex stimulation activates the anterior cingulate region. This region is involved in the coding of affective, emotional and cognitive components of pain, which suggests that part of the efficacy of this technique is related to a modification of these various components.
The selection of candidates for motor cortex stimulation must comply with the usual criteria for the management of patients with chronic pain and must be based on a multidisciplinary approach. Recent studies have shown that repetitive transcranial magnetic stimulation is predictive of the efficacy of the procedure and can therefore guide patient selection. Technically, the procedure has become much more precise in the delineation of the cortical target. MRI linked to neuronavigation can now be considered to be essential. Intraoperative electrophysiology is also necessary to verify anatomical data by studying

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somatosensory evoked potentials and motor responses to cortical stimulation. Functional MRI is particularly useful to verify the somatotopic distribution within the motor cortex in patients with severe sensorimotor deficits.
Adjustment of stimulation parameters remains largely empirical, but the development of modelling procedures provides a better understanding of how the current diffuses within the cortex. These models have largely validated certain effective stimulation parameters established empirically on the basis of clinical experience.
The clinical results of motor cortex stimulation are still variable according to the team and the indications (between 40% and 80% of good results). Further scientific studies to provide a better understanding of the mechanism of action and modelling studies allowing more reliable adjustment of stimulation parameters could help to improve the clinical results.

Learning Objectives

1. Explain the significance of using a good technique to place the electrodes on the adequate cortical target;
2. Explain why the technique needs to include neuronavigation and intraoperative electrophysiology;
3. Describe the mechanisms of action which may improve the selection of patients and the adjustment of stimulation parameters.

1540 – 1600 Marquesa Ballroom I-II (16)
Deep Brain Stimulation in Epilepsy
Ashwini Sharan, MD
Thomas Jefferson University
Department of Neurosurgery
Philadelphia, Pennsylvania USA

Francisco Velasco, MD
Epilepsy Clinic
Unit for Stereotaxic and Functional Neurosurgery
Mexico General Hospital, Mexico City, Mexico.

Ana Luisa Velasco MD, PhD contributed significantly to this presentation.

Abstract
Patients and Methods: All patients had long history (>3 years) of difficult to control seizures in spite of adequate medical treatment. They were not candidates for ablative procedures because seizures overlapped eloquent areas, they were bilateral or multifocal or had not evidence of focal onset. They were treated by bilateral cerebellar stimulation (5 cases); centro-median thalamic stimulation (53 cases), hippocampal stimulation (10 cases) and foci in eloquent area stimulation (3 cases). Transoperative X Ray films helped to place electrodes over parasagittal cerebellar cortex. Stereotactic placements guided by ventriculography or image fusion and electro cortical evoked recruiting responses help the placement of DBS electrodes in the centromedian (CM) thalamus. Image fusion guided and EEG recordings help the placement of electrodes in the hippocampal foci. Stimulation parameters adjusted to deliver less than 4 µC/sg.CM/phase in cycling mode.

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Results: Number of seizures decreased significantly with cerebellar stimulation (P<0.01), CM stimulation (P<0.001) and stimulation at the epileptic foci (P< 0.001). Double blind protocols designed at the onset of stimulation without crossover demonstrated that seizure reduction were significantly different during stimulation periods (p<0.01). No adversive effects were related with electrical stimulation, but with skin erosion over the stimulations hardware. Best results were found in those cases with correct stereotactic placement corroborated by electrophysiological tests.

Conclusions: DBS stimulation is an alternative to treat epileptic patients not candidates for ablative procedures.

Learning Objectives
At the conclusion of this presentation, participants should be able to:
1. Determine efficacy and safety of deep brain stimulation (DBS) in the treatment of convulsive disorders;
2. Establish indications for different places for DBS and prognostic factors associated with favorable outcome.

1600 – 1630
Break

1630 – 1650 Marquesa Ballroom I-II (16)
DBS for Cluster Headache
Gianni Broggi, MD, PhD
Istituto Nazionale Neurologico "C.Besta"
Milan, Italy

1650 – 1715 Marquesa Ballroom I-II (16)
Question and Answer

1715 – 1800
Margaritas

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0800 - 1200 Princessa Ballroom B-C (13)
Plenary Session: FES Day
Paul Meadows, PhD – Session Chair
Boston Scientific
Valencia, California USA

0800 - 0840 Princessa Ballroom B-C (13)
Upper Limb Post-stroke Rehabilitation: Implantation of 5-7 Microstimulators and Effects
Ross Davis, MD
Alfred Mann Foundation
Valencia, California USA

Abstract
Introduction: Seven Participants (3 females/4 males) with post-stroke arm weakness and spasticity were chosen and had baseline quantitative testing. Their stroke occurred at a mean of 3.9yrs (1.1 to 10.5yr.), mean age: 45yrs (32-67yrs). 5-7 radio-frequency microstimulators (RFM; 2.4mm x17mm) were implanted on selected branches of the radial nerve/motor-point, and underwent home-based programmed stimulation to extend elbow, wrist and fingers to augment functional activities for 1 hour/day for 12 weeks (Phase-1), then had quantitative testing.

Materials and Methods: First implantation was in April 2005 and the seventh in March 2006. Pre-operatively, implantation sites were identified by needle EMG. Under local anesthesia, using 5mm incisions, targeted nerve/motor-points were identified using an inserted probe with stimulation, and then an RFM was inserted using developed introducer and ejection tools. RFMs with attached suture could be retrieved during surgery and up to 8 days. Each device receives power and activation commands via a RF inductive link from the 2 externally placed cuff-coils connected to the Control Unit. Initially a total of 41 RFMs (5-7/subject) were implanted. Each surgery session took 3.5 to 6 hrs (av:4.9hr). In participant #4, 5 months post-surgery, 2 more RFMs were inserted in 2 triceps' sites for elbow extension.

Results: Mean thresholds of 2.2 µC/sqcm/phase indicate that RFM cathodes were equal or <2mm from their target sites. No RFMs have failed. No infections have occurred. All participants completed 12 weeks of stimulation (Phase-1). Results are presented as mean (SD) and % changes in Action Research Arm Test: 4.9 (7.89) 21% and Target tracking: 57.3 (48.65) 70%. Significant reduction occurred in motor impairment measured by the Fugl-Meyer (P=0.027).

Conclusion: The study has demonstrated feasibility and safety of using implanted microstimulators in post-stroke rehabilitation and has shown a mean improvement across all participants during Phase-1. Three participants whose stroke occurred <2 years showed more improvement.

Acknowledgements
This project has been funded by the non-profit Alfred Mann Foundation.

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Learning Objectives
At the conclusion of this lecture, participants should be able to:
1. Describe the technique of implanting and controlling microstimulators for Functional Electrical Stimulation (FES) in the rehabilitation of participants with post-stroke arm paresis;
2. Asses the efficacy and safety of long-term use of microstimulators;
3. Appraise the feasibility of using implanted microstimulators in the upper limb of participants with post-stroke hemiparesis to produce effective and safe functional improvements for daily living.

0840 – 0920 Princessa Ballroom B-C (13)
Fully Implanted Nerve Sensing and Stimulation System for Treatment of Paralysis After Hemiplegia or Related Neurological Disorders
J. Andrew Hoffer, PhD
Professor of Kinesiology
Simon Fraser University
Burnaby, British Columbia Canada

Abstract
Injuries or diseases of upper motor neurons can commonly result in permanent gait abnormalities and compromised postural control. Persons who have hemiplegia from a stroke, spinal cord injury, traumatic brain injury, cerebral palsy or multiple sclerosis often either drag the paralyzed foot and toes or engage in a high-stepping walk. This condition, called foot drop, is caused by weakness or paralysis of flexor muscles in the affected leg, particularly the anterior calf muscles that lift the foot and results in slow, asymmetric, energy-costly walking, increased risk of falling, and can lead to spine pathologies and chronic pain.

Foot drop is such patients is traditionally treated with an ankle-foot orthosis (AFO) that braces the foot at a fixed angle to facilitate toe clearing for walking. AFOs have limitations in that they can be heavy, hot, cause pain, irritate the skin, cause pressure sores, interfere with active ankle plantarflexion, and are cosmetically unacceptable to many patients. A more functional alternative than AFO's is to electrically stimulate the peroneal nerve appropriately to lift the foot as needed for walking. Electrical stimulation has direct orthotic effects by lifting the foot for walking and long-term therapeutic effects by reversing the disuse atrophy of the ankle dorsiflexor muscles, increasing muscle force output and fatigue resistance, modulating reflex pathways.

Three types of devices provide functional electrical stimulation (FES) for foot drop. External devices are totally outside the body, with surface electrodes placed on the skin below the knee to stimulate the peroneal nerve. Semi-implanted devices include external components (power supply, control circuitry, sensors and external radiofrequency antenna that sends stimulation commands) and internal components (receiving antenna, and stimulating electrodes permanently implanted near, in or on the peroneal nerve). A fully implanted device is like a cardiac pacemaker, with no external components; its power supply, control circuitry, sensors and communications antenna are inside a implanted pulse generator (IPG), stimulating leads terminate near, in or on the peroneal nerve, and sensing leads terminates in electrodes on the tibial nerve to sense afferent nerve signals used as feedback for closed-loop control of stimulation.

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This lecture will summarize the benefits, risks and limitations of each of these 3 approaches for treating foot drop with FES and also the basic properties, requirements, indications and contraindications for using fully implanted nerve stimulating and sensing electrodes in clinical applications.

Learning Objectives
At the conclusion of this lecture, participants should be able to:
1. Recognize the basic gait and balance disorders and mobility assistance needs of subjects with hemiplegia;
2. Contrast the benefits, risks and limitations of current methods that treat hemiplegic gait and posture;
3. Differentiate the benefits, risks and limitations of using implanted electrodes to stimulate peripheral nerves;
4. Describe the benefits, requirements, risks and limitations of sensing nerve signals for clinical applications.

0920 – 1000 Princessa Ballroom B-C (13)
Motor Cortex Stimulation for Stroke Rehabilitation: Update on the Everest Study
Robert Levy, MD, PhD
Northwestern Medical Faculty Foundation, Inc.
Dept. of Neurological Surgery
Chicago, Illinois USA

Abstract
This course will provide an overview of the basic and clinical science supporting the use of motor cortex stimulation combined with rehabilitation for motor recovery following ischemic stroke. The Everest study, a multicenter, prospective, randomized, placebo controlled Phase III pivotal trial, will be described in detail and discussed. The primary endpoint of the study (4 week outcome data) will be reached by October 2007 and these results will be presented.

Learning Objectives
At the conclusion of this lecture, participants should be able to:
1. Restate the clinical benefits of using a combination of motor cortex stimulation and rehabilitation for motor recovery following ischemic stroke.

1000 – 1030
Break

1030 – 1110 Princessa Ballroom B-C (13)
Functional Electrical Stimulation Therapy: Retraining Reaching and Grasping Functions in Severe Stroke Patients
Milos R. Popovik
Toronto Rehabilitation / IBBME
University of Toronto
Toronto, Ontario Canada

Abstract
During the course of rehabilitation hemiplegic patients who have Chedoke McMaster Stages of Motor Recovery scores 4 and 5 measured three weeks after onset of stroke often improve their arm and hand function to the point that they can later use it in the

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activities of daily living (ADL) (mild arm and hand paralysis). On the other hand, hemiplegic patients who have Chedoke McMaster Stages of Motor Recovery scores 1 and 2 measured three weeks after onset of stroke, during the course of rehabilitation seldom improve their arm and hand function, and when they do, the improvements are not sufficient to allow these patients to use the arm and hand in ADL (severe arm and hand paralysis). A new rehabilitation technique that can improve both reaching and grasping functions in acute and long-term hemiplegic patients with severe unilateral arm paralysis has been proposed. A neuroprosthesis that applies surface electrical stimulation technology was used to retrain arm and hand functions. Patients who were treated with the neuroprosthesis were compared to those patients who were administered only standard physiotherapy and occupational therapy (controls). The treated and control patients had approximately the same time allocated for arm and hand therapy. The patients treated with the neuroprosthesis significantly improved their reaching and grasping functions, and were able to use them in ADL. However, the majority of the control patients did not improve their arm and hand functions significantly, and were not able to use them in ADL.

Learning Objectives
At the completion of this presentation, participants should be able to:
1. Discuss the concept behind Functional Electrical Stimulation (FES) Therapy;
2. Explain how FES therapy is implemented in a clinical setting;
3. Discuss the practical aspects of FES therapy with respect to treating severe stroke patients;
4. Present latest results of the randomized control trial.

1110 – 1200 Princessa Ballroom B-C (13)
Transcranial Magnetic Stimulation: A Non-invasive Method of Brain Stimulation
Felipe Fregni, MD, PhD
Assistant Professor of Neurology
Harvard Medical School
Beth Israel Deaconess Medical Center
Boston, Massachusetts USA

Abstract
Electromagnetic brain stimulation was first investigated in the late 19th century. It was not until the mid-1980s, however, that Barker and colleagues introduced transcranial magnetic stimulation (TMS), having solved the technical challenges involved in bridging the scalp and skull with a magnetic field pulse of sufficient strength and rapid enough change over time. TMS uses the principle of electromagnetic induction to focus induced currents in the brain. Single pulses of current can be of sufficient magnitude to depolarize neurons transiently, but when these currents are applied repetitively—an approach known as rTMS—they can modulate cortical excitability, decreasing or increasing it depending on the parameters of stimulation, beyond the duration of the train of stimulation.

There is mounting evidence for the efficacy of rTMS in various neurological conditions. Experience in various clinical trials illustrates different fundamental uses of TMS in neurological disorders: modulation of activity in the targeted cortex (such as in focal epilepsy); modulation of activity in a dysfunctional corticosubcortical network (such as in Parkinson's disease); restoration of adaptive equilibrium in a disrupted network, guiding plasticity for best behavioral outcome (such as in stroke); and suppression of plastic

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changes for functional advantage (such as in chronic pain). To date, findings are encouraging and randomized clinical trials show positive results with moderate to large effects in some cases, but the number of trials is still insufficient to allow endorsement of widespread use of these techniques, despite the great margin of safety if appropriate guidelines and precautions are followed.

Learning Objectives:
At the completion of this presentation, participants should be able to:
1. State the basic principles of brain stimulation with rTMS;
2. Identify the advantages and disadvantages of rTMS;
3. Summarize the clinical effects of this technique in neuropsychiatry.

1200 – 1415 Break

1415 - 1715 Marquesa Ballroom I-II (16)
SCS for Visceral Pain
Elliot Krames, MD - Session Chair
Pacific Pain Treatment Center
San Francisco, California USA

1415 – 1600 Marquesa Ballroom lll-lV (16)
Braingate – Positive Feedback
Gerhard Friehs, MD - Session Chair
Bio Med Clinical Neuroscience
Brown University
Providence, Rhode Island USA

1415 - 1600 Atlantes
Commercial Symposium – see Non-CME Syllabus for information

1415 – 1440 Marquesa Ballroom I-II (16)
Nociception of the Heart
Robert D. Foreman, PhD, FAHA
University of Oklahoma Health Sciences Center
College of Medicine
Department of Physiology
Oklahoma City, Oklahoma USA

Abstract
Spinal cord stimulation (SCS) has been used to treat patients with severe angina pectoris that is refractory to conventional therapies. Success rates achieved with SCS for angina pectoris is in excess of 80%. Patients treated with this therapy experience reduced severity and frequency of anginal episodes, and in some cases these episodes are eliminated. In addition to pain relief, clinical studies demonstrate that SCS increases exercise tolerance, changes ischemia related ECG (ST depression) and improves the quality of life. The challenge is to understand the neural mechanisms underlying angina pectoris and other cardiac disorders that contribute to the success of SCS for treating heart disease. To address this challenge research is being conducted to determine how SCS depends on the neural hierarchy of the brain, spinal cord and heart to modulate the complex mechanisms underlying such devastating conditions as refractory angina pectoris, cardiac arrhythmias, and myocardial ischemia. Research has focused on spinal

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processing of cardiac nociceptive impulses and as a result these studies have identified the C1-C2 and the T2-T4 segments of the spinal cord as critical for processing information in the neural hierarchy. Evidence also supports the idea that SCS may alter the function of the intrinsic cardiac nervous system, reduce infarct size, and decrease atrial and ventricular arrhythmias. This presentation will briefly review the efficacy of SCS in relieving angina pectoris, provide an overview of the spinal processing of cardiac nociceptive information and the neural mechanisms of referred pain in the thoracic and cervical spinal cord, and examine the effects of SCS on cardiac function.

Learning Objectives
At the conclusion of this lecture, participants should be able to:
1. Review the efficacy of neuromodulaiton in relieving angina pectoris;
2. Examine physiological mechanisms of the spinal neural hierarchy that modulate cardiac nociception by SCS;
3. Compare and contrast the effects of neuromodulation on the heart.

1415 – 1440 Marquesa Ballroom III-IV (16)
Development of Neural Interface Systems: Signals for Control and Diagnosis
John P. Donoghue, PhD
Department of Neuroscience
Brown University
Providence, Rhode Island USA

Abstract
This talk will describe the preclinical development of neural interface systems to restore lost function for those with paralysis. Types neural sensors and signals available as control signals for neural prosthesis systems will be discussed. In addition, the presentation will describe animal studies leading up to recent human trials of neural prosthesis systems in paralyzed humans. Finally, the talk will cover issues related to long term stability of neural interfaces and the potential use of this technology in other applications.

Learning Objectives
1. At the conclusion of this lecture, participants should be able to:
2. Explain the overall design concept of neural interface systems;
3. Review the types of sensors being developed for neural interfaces;
4. Discuss the different types of neural electrical signals and the information they provide;
5. Update the current status of non-human primate work in the development of neural prosthesis systems.

1440 – 1500 Marquesa Ballroom I-II (16)
Mechanisms of Electrical Neuromodulation in the Treatment of Chronic Refractory Angina Pectoris
Mike J. L. DeJongste, MD, PhD, FESC
Department of Cardiology
Thoraxcenter
University Medical Center Groningen
Groningen, Netherlands

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Abstract

Background: Patients are considered suffering from chronic angina pectoris refractory to standard treatment when they experience disabling pain, resulting from myocardial ischemia, unresponsive to standard medication and revas¬cularization. Making use of quality of life assessment and pain questionnaires, many observational and randomized studies testify that this unmet medical identity can be successfully treated with Electrical Neuromodulation (EN). In addition, reduction of myocardial ischemia through EN has been shown by right atrial pacing, exercise stress testing, ambulatory ECG, Positron Emission Tomography (PET), nuclide perfusion scan and coronary flow measurement.

Mechanism of action of EN in the nervous system in relation to the anti-angina effect, in addition to the "gate control" model for the spinal cord, EN stabilizes the increased activity of the firing rate of intrinsic cardiac neurons at the heart, following coronary occlusion. PET studies and studies with c-fos, a marker of neuronal activity, demonstrate that EN also modulates neurons in the cognitive centers of the brain. Further, during an acute myocardial infarction EN is not able to suppress angina. Finally, clinical studies report that EN stimulates production of endorphins in the heart and that EN also affects adenosine handling. Since adenosine has vasodilatory effects and is involved in pain transmission, adenosine may be a very important substance in coupling the involved neuronal (antianginal) and cardiac (antiischemic) mechanistic interactions.

Mechanism of action of EN on the heart: It is not clarified whether alterations in coronary flow during EN are related to modulation of the b-sympathetic nervous system, since in clinical studies no significant change in heart rate variability was reported. Further, EN does not affect catecholamine spill-over. However, EN may modulate ischemia through influencing both, the a-sympathetic nerves and the vagal balance.
The increased angina threshold was first emphasized by a study in which patients with refractory angina and EN were stressed by right atrial pacing until ischemic threshold. This rise in ischemic threshold and the delayed onset of angina during EN, are thought to be related to redistribution of coronary blood flow from normal perfused (non-ischemic) to impaired perfused (ischemic) myocardial regions, causing a homogenization of myocardial perfusion and so improvement of ischemic tolerance. Ischemic tolerance is determined by both, preconditioning and collateral recruitement in the heart. Both, preconditioning and collateral recruitement has been recently reported to be involved in EN, following occlusion of a coronary artery.

Conclusion: EN is an effective and safe method for relief of severe angina in patients with refractory angina. The underlying antianginal mechanism are thought to result from differential resetting of the neural hierarchy in cardiac control. The outcomes of the cardiac indices suggest EN to exert an antiischemic effect related to an improvement in both angina and ischemic threshold. The ischemic threshold has been found to improve through activation of mechanisms which induce both preconditioning and recruitment of collaterals.

Learning Objectives

At the conclusion of this lecture, participants should be able to:

1. Define indications and selection criteria for Electrical Neuromodulation, used as an adjunct therapy, in patients suffering from chronic refractory angina;
2. Review clinical results of Electrical Neuromodulation in patients with chronic refractory angina;

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3. Evaluate underlying neurological mechanisms of action following Electrical Neuromodulation in patients with chronic refractory angina.

1440 – 1500 Marquesa Ballroom lll-lV (16)

Early Pilot Clinical Trial Experience with an Intracortically-based Neural Interface System for People with Paralysis

Leigh R. Hochberg, MD, PhD
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Department of Veterans Affairs
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Harvard Medical School
Boston, Massachusetts USA
Dept. of Neuroscience, Brown University
Providence, Rhode Island USA

Abstract

Neural interfaces are poised to revolutionize our ability to restore lost function to people with neurologic disease or injury. More than 40 years of fundamental, largely NIH-funded research has yielded considerable understanding of how the activities of single neurons in motor cortex are related to limb movement. Over the past decade, technologies to record the individual and simultaneous activities of dozens to hundreds cortical neurons have yielded new understandings of cortical function in movement, vision, cognition, and memory. This preclinical research, generally performed with healthy, neurologically intact non-human primate subjects, has demonstrated that direct, closed-loop, neural control of virtual and physical devices can be achieved [1-5, and others]. Recently, this exciting research has been translated into initial pilot clinical trials (IDE) of the BrainGate Neural Interface System (Cyberkinetics Neurotechnology Systems, Inc.). These pilot trials examine the feasibility of persons with tetraplegia controlling a computer cursor simply by imagining movement of their own hand.

To date, four participants with tetraplegia have been enrolled in the BrainGate trials; two people with cervical spinal cord injury, one person with a brainstem stroke, and one person with advanced motor neuron disease (amyotrophic lateral sclerosis, or Lou Gehrig's Disease). Two of these participants could not speak due to their neurologic disease. Utilizing signals from motor cortex recorded via a chronically implanted intracortical array of 96 microelectrodes, neuronal activities are transmitted via cabling to a computer and then decoded in real time into either the movement of a cursor or control over other external devices. Initial results from the first participant in the study [6] revealed that despite transection of the cervical spinal cord and more than two years' opportunity for rearrangement of motor somatotopy, neurons in the "hand area" of motor cortex continued to modulate their activity immediately upon the imagined or intended movement of the paralyzed hand. By harnessing and decoding these natural movement signals, the first participant was able to play video games, read simulated email, open and close a prosthetic hand, and manipulate a rudimentary robotic arm and hand. Over the past year, advances in decoding strategies have yielded improved neural cursor control, and multi-state decoding has permitted a "point and click" interface. While there are challenges ahead (e.g., demonstration of signal stability over years, fully implantable neural interface systems), there is great potential for this and related

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neurotechnologies to re-enable the communication, mobility, and independence of persons with physical disability.

Learning Objectives
At the conclusion of this lecture, participants should be able to:
1. Describe progress made and challenges ahead for intracortically-based neural interface systems;
2. State basic inclusion/exclusion criteria for an ongoing pilot clinical trial of the BrainGate Neural Interface System;
3. Discuss other potential clinical uses for chronic intracortical recording systems.

References

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1500 – 1520 Marquesa Ballroom I-II (16)
SCS for Visceral Pain: The Scientific Evidence
Elliot Krames, MD
Pacific Pain Treatment Center
San Francisco, California USA

Abstract
Early animal and human evidence existed for a postsynaptic dorsal column pathway (PSDC) for visceral nociception, that when lesioned, decreased pain of terminal illness. There have been recent anecdotal reports in the literature that spinal cord stimulation (SCS) reduces pain of visceral nociception. I will present here a review of the literature supporting a hypothesis that SCS might work by modulating information through the spinothalamic tracts and PSDC.

Learning Objectives
At the conclusion of this lecture, participants should be able to:
1. Recognize that chronic visceral pain is neuropathic in nature and therefore amenable to neuromodulation by spinal cord stimulation;
2. Explain the relationship between the gut, the spinal cord and the brain;
3. Recognize that the post synaptic dorsal column pathway is integral to modulating nociceptive information from the viscera and can be, in turn, modulated by spinal cord stimulation.

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1500 – 1520 Marquesa Ballroom lll-lV (16)
Decoding Plan Activity From Neuronal Ensembles in Human and Non-human Primates
Jaimie M. Henderson, MD
Director, Stereotactic and Functional Neurosurgery
Stanford University School of Medicine
Stanford, California USA

Abstract
Several methods have been developed for the control of neuroprosthetic devices, using both invasive and noninvasive techniques. Recording of multiple cortical neurons with closely-spaced microelectrodes has yielded high-quality signals which can be used for the control of cursors, robotic arms, or other effectors. Decoding of movement-related activity from primary motor cortex (M1) to drive an on-screen cursor has been effectively demonstrated in paralyzed humans. Our group has focused on extracting planning information from dorsal premotor cortex (PMd) in non-human primates, which can theoretically improve prosthetic performance by many-fold over current systems based solely on M1 decoding. Data will be presented from both human and non-human primate experiments showing rapid decoding, high-quality cursor control, an the ability to record from freely-moving subjects.

Learning Objectives
At the completion of this presentation, participants should be able to:
1. Compare various brain targets for the control of neuroprosthetic devices;
2. Describe an experimental paradigm for recording neuronal ensemble activity from dorsal premotor cortex in non-human and human primates;
3. Discuss the present state of technology for acquiring and decoding plan activity for high-performance neuroprosthetics.

1520 – 1540 Marquesa Ballroom I-II (16)
SCS for Visceral Pain: A Review of the Literature
Leonardo Kapural, MD, PhD
Pain Management Department
Cleveland Clinic
Cleveland, Ohio USA

Abstract
Spinal cord electrical stimulation (SCS) has been used for the treatment of neuropathic pain of various etiologies, ischemic pain and complex regional pain syndrome. In animals, electrical SCS can suppress viscero-motor response to colon distension (Greenwood-Van Meerveld et al., 2003). A few recent case reports suggested effectiveness of SCS in suppression of long-standing visceral and non-visceral abdominal or truncal pain in human subjects (Krames and Moussad, 2005; Khan et al., 2005, Kapural et al., 2006, Kapural, 2006, Tiede et al, 2006).

Although, a significant number of patients with severe visceral pain will transiently respond to visceral nerve blocks and radiofrequency ablation, substantial long-term pain relief usually is lacking. SCS therefore may be a welcome alternative or additional treatment for moderate to severe chronic visceral epigastric pain. During this panel patophysiology of visceral pain will be described, possible mechanisms of

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neuromodulation will be discussed and clinical results and future directions in treatment of abdominal and visceral pelvic pain using neuromodulation will be detailed.

Learning Objectives
After completing this activity, the participant should be able to:
1. Summarize the pathophysiology of chronic visceral pain syndromes and physiological basis of neuromodulation for visceral pain;
2. Recognize new interventional techniques in treatment of chronic pelvic and abdominal pain;
3. Discuss clinical results of the neuromodulation for treatment of chronic visceral pain.

1520 – 1540 Marquesa Ballroom III-IV (16)
Microelectrode Recordings of Human Cortical Activity in Epilepsy
Sydney S Cash, MD PhD
Massachusetts General Hospital
Harvard Medical School
Boston, Massachusetts USA

Abstract
Epilepsy remains a significant disease affecting some 50 million people worldwide. Unfortunately, our medical and surgical treatments are often ineffective and may carry significant side-effects. Our ability to develop new therapeutic approaches to this disease has been limited by a paucity of detailed physiological information of human epilepsy in particular. New developments in microelectrode recording techniques, coupled with advances in computational capabilities have opened a new frontier in understanding human cortical activity. In particular, we now have the ability to record the activity of multiple single neurons in patients undergoing evaluation for epilepsy. In this presentation we will discuss the application of these new microelectrode array technologies to increasing our understanding of what characterizes the epileptic area of the cortex, how seizures start, spread and stop. Most importantly, we will also examine the ways these new devices and the information obtained can be used for the construction of novel neuroprosthetic devices for predicting, detecting and interrupting seizures.

Learning Objectives
At the conclusion of this lecture, participants should be able to:
1. Summarize the potential of new technologies to record neuronal activity in human cortex in the acute and even chronic setting;
2. Appreciate the possibilities these new types of recordings offer for brain-computer interfaces overall;
3. Relate the possibilities these devices offer for understanding and ultimately treating neurological disorders in general and epilepsy in particular.

1540 – 1600 Marquesa Ballroom I-II (16)
Urological Disorders and Neuromodulation
Magdy M. Hassouna, MD, PhD
Toronto Western Hospital
Toronto, Canada

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Abstract

Sacral root neuromodulation is one of the relatively recent concepts for treatment of various voiding and storage dysfunction. The modality is getting wide acceptance among the international urology community. The principles of this modality have been laid by Tanagho and Schmidt early in 1980s.1,2 Since then over 6500 patients have been implanted by neuroprosthetics for treatment of various dysfunctions. Several reports have been published addressing different aspects. Indications have expanded. They include urge incontinence and sensory urgency. , , idiopathic chronic urinary retention , , pelvic pain 4, 7 and interstitial cystitis.

The neuromodulation is especially beneficial for women for unclear reasons. The reason could be that women are more vulnerable than men to pelvic pathology. Many of female patients showed the symptoms of voiding dysfunction following gynecological or obstetric procedures.

Patients in any of the previously mentioned categories of bladder dysfunction have to undergo a screening test called "Percutaneous nerve evaluation (PNE)". In this test, a temporary wire electrode is inserted in the S3 foramen. The patient is sent home with an external pulse generator for a few days. Responders are then implanted with a permanent sacral foramen implant and an implantable pulse generator (IPG).

Percutaneous nerve evaluation - This test was first described as a clinical test to evaluate detrusor innervation. The technique that was used previously was different from recent publications. The test was done under local anesthesia and the patient was positioned laterally. The aim was to test the response of the urinary bladder, manifested in pressure changes, to S3 electrostimulation in candidates for neuroprothetic implants designed for bladder evacuation. The patient is positioned prone with slight flexion of the hips. S3 foramen is located one fingerbreadth off the midline at the level of the sciatic notch. The entire procedure is conducted under local anesthetic. A specially designed needle 23-G is used to probe the foramen and test the sacral nerve root. The recommended angle is 60o to the skin. The stimulation current used ranges between 3-5 mA, 15 Hz and 200 ms. Each foramen is separated with one finger width in the vertical plane from adjacent foramina. Once the desirable somatic response was found, an electrode wire is passed through the needle sheath and secured in place by means of adhesive tapes.

Somatic responses to sacral roots neurostimulation -Sacral roots S2-4 are responsible for nervous supply of most of the pelvic organs. They give rise to both the pelvic and pudendal nerves. The pelvic nerve is the one carrying the autonomic innervation while the pudendal carries the somatic innervation. In addition, few somatic fibers arise from the S2 & 3 and run in close proximity to the pelvic nerve to supply the levator muscle and the striated rhabdosphincter around the membranous urethra.2

The sacral root of interest to us is the S3 root. Typical response of stimulating this nerve is seen in the perineum and the foot. Electrostimulation of this root results in contraction of the detrusor, levator and to a lesser extent the urethral sphincter in addition to the big toe muscles. During PNE, this response is translated into a bellow reflex, which is inward movement of the anus and deepening of the gluteal cleft. Subjectively, the patient feels pulling sensation in the rectum with variable sensation in the labia. Stimulation of S2 produces contraction of more superficial perineal muscles causing clamping like effect. It may cause some sphincteric contraction but not detrusor

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response. Furthermore, it causes planter flexion of the foot and lateral rotation of the leg. S4 causes bellow like action without any foot movement. Occasionally there is an overlap between the dermatomes.7

Subchronic wire test - After obtaining the desirable response and securing the wire in place, the patients are sent home with the wire coupled to a portable pulse generator for a 5-7 day period of outpatient stimulation trial. Responders are those patients that show considerable improvement of their symptoms during the subchronic testing period. The choice of the implant side is dependent on the side that gave best response.7

Urge incontinence and sensory instability - Urge incontinence and sensory instability are one of the first indications of this modality. The principle of this indication came from the observation of the ability to restore the reservoir function of patients with suprasacral spinal cord injury during sacral root neurostimulation. In that study, the primary aim of sacral root stimulation was to induce voiding. It has to be mentioned that most the patients in this study have undergone extensive dorsal rhizotomy, which may be the main reason for restoration of the continence.

In 1995, Bosch and Groen reported their results in 18 implanted patients with urge incontinence secondary to detrusor instability. The voiding diaries of these patients showed a highly significant drop in the leakage episodes and frequency with a significant increase in the average voided volume. The number of protective pads/day dropped significantly as well. The effect was durable as 13 patients who have been followed up for more than two years maintained the same initial improvement. Urodynamically, the bladder instability disappeared in 8 of the 18 patients while the other ten showed an increased infused volume to first uninhibited contraction and to the maximum uninhibited contraction. This was associated with increased bladder volume at capacity and first sensation. There was no complete correlation between the urodynamic findings and the patient symptomatology. Three of the nine patients who were completely dry showed persistence of the uninhibited contractions while two of the nine who were not completely dry showed a stable bladder.3

Thon and colleagues provided similar results. Out of 20 patients with urge urinary incontinence 17 of them showed an improvement of more than 50% compared to the base line which persisted for more than a year of follow-up.7 Elabbady and colleagues presented their results in patients with urgency frequency and/or urge incontinence. Frequency improved by 73%, urgency by 42% and incontinence by 50%. Urodynamically, bladder instability disappeared in one patient and bladder volume at first sensation increased by 50%.

In more recent studies, sacral Neuromodulation have shown significant improvement in the quality of life in patients with urge frequency and incontinence. ,
Idiopathic non-obstructive chronic urinary retention - This is another major indication for sacral root neuromodulation. Most recent studies point to an increase in the voided volume and decrease in the number of catheterization in 80% of patients. Average voided volume improved significantly and was associated with marked reduction in the residual urine. This was associated with significant improvement in the uroflowmetry data. In a recent multicenter trial, the authors have shown that 69% of patients with chronic urinary retention have eliminated the use of catheterization altogether. The follow up period was over 18 months.

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Miscellaneous indications - Pelvic pain or discomfort presented a very common symptom associated with other storage or voiding dysfunctions. In many of the publications for sacral root neuromodulation, associated pelvic pain has improved remarkably. This improvement ranged from 85% to 90% when post implant status was compared to the base line.

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Learning Objectives

At the conclusion of this lecture, participants should be able to:

1. Describe indications for sacral root neuromodulation;
2. Summarize the clinical benefits of sacral root neuromodulation treatment for urological disorders.

1540 – 1600 Marquesa Ballroom III-IV (16)
Question and Answer

1600 - 1630
Break

Tuesday December 11, 2007

1630 – 1650 Marquesa Ballroom I-II (16)
Gastric Electrical Stimulation for Visceral Pain
Jiande Chen, PhD
University of Texas, Medical Branch
Galveston, Texas USA

Abstract
According to stimulation parameters (pulse width), gastrics electrical stimulation can be classified in to two major categories: short pulses (with a pulse width in the order of μs) and long pulses (with a pulse width in the order of ms). Long pulse GES has been reported to alter gastrointestinal functions and thus has therapeutic potentials for various gastric motility disorders and obesity. Short pulse GES has been reported to be able to improve symptoms such as nausea/vomiting and visceral pain, possibly mediated through the vagal and sympathetic pathways.

Clinically short pulse GES has been applied to treat nausea and vomiting in patients with gastroparesis (delayed gastric emptying), a method called Enterra Therapy®. In this method, a pair of stimulation electrodes are placed on gastric serosa and connected to a pulse generator placed in a subcutaneous pouch in the abdomen. Over 1000 patients with gastroparesis at various medical centers have been treated using this method. An overall improvement nausea and vomiting has been noted in about 50-75%. Possible mechanisms involving the vagal and central pathways have been reported.

Possible applications of short pulse GES for the treatment of visceral pain have also be explored in recent animal studies. In one study, gastric electrical stimulation with various stimulation parameters was applied to treat visceral pain/discomfort induced by gastric distention in dogs. Interesting results were obtained and will be presented in this lecture.

In another study, GES was explored to treat visceral pain in a rodent model of visceral hypersensitivity induced by intragastric injection of acetic acid. Effects of GES with different stimulation sets on visceral pain were investigated using electromyographic recordings. Possible methanisms involving the spinal sympathetic pathway were also studied.

Learning Objectives
At the conclusion of this lecture, participants should be able to:
1. Describe basic methods of gastric electrical stimulation;
2. State possible effects and mechanisms of gastric electrical stimulation;
3. Summarize the physiology and pathophysiology of gastric hypersensitivity.

1650 – 1715 Marquesa Ballroom I-II (16)
Question and Answer

Wednesday December 12, 2007

0800 – 1200 Princesa Ballroom B-C (13)
Plenary Session: Stimulation of Organs Day
Elliot Krames, MD - Session Chair
Pacific Pain Treatment Center
San Francisco, California USA

0800 – 0840 Princesa Ballroom B-C (13)
Functional Electrical Stimulation Therapy: Retraining Reaching and Grasping Functions in Severe Stroke Patients
Magdy M. Hassouna MD PhD
Toronto Western Hospital
Toronto, Canada

Abstract
During the course of rehabilitation hemiplegic patients who have Chedoke McMaster Stages of Motor Recovery scores 4 and 5 measured three weeks after onset of stroke often improve their arm and hand function to the point that they can later use it in the activities of daily living (ADL) (mild arm and hand paralysis). On the other hand, hemiplegic patients who have Chedoke McMaster Stages of Motor Recovery scores 1 and 2 measured three weeks after onset of stroke, during the course of rehabilitation seldom improve their arm and hand function, and when they do, the improvements are not sufficient to allow these patients to use the arm and hand in ADL (severe arm and hand paralysis). A new rehabilitation technique that can improve both reaching and grasping functions in acute and long-term hemiplegic patients with severe unilateral arm paralysis has been proposed. A neuroprosthesis that applies surface electrical stimulation technology was used to retrain arm and hand functions. Patients who were treated with the neuroprosthesis were compared to those patients who were administered only standard physiotherapy and occupational therapy (controls). The treated and control patients had approximately the same time allocated for arm and hand therapy. The patients treated with the neuroprosthesis significantly improved their reaching and grasping functions, and were able to use them in ADL. However, the majority of the control patients did not improve their arm and hand functions significantly, and were not able to use them in ADL.

Learning Objectives
1. Discuss the concept behind Functional Electrical Stimulation (FES) Therapy;
2. Explain how FES therapy is implemented in a clinical setting;
3. Discuss the practical aspects of FES therapy with respect to treating severe stroke patients;
4. Present latest results of the randomized control trial.

0840 – 0920 Princesa Ballroom B-C (13)
Review of Neuromodulation for Cardiac Disorder (non-CME)
Marc Penn, MD PhD
Bakken Heart-Brain Institute, Director
Cleveland Clinic
Cleveland, Ohio, USA

Wednesday December 12, 2007

0920 – 1000 Princesa Ballroom B-C (13)
Electrical Stimulation for Gastrointestinal Disorders
Jiande Chen, PhD
University of Texas
Medical Branch
Galveston, Texas

Abstract
Gastrointestinal electrical stimulation (GIES) has been intensively studied during the recent years and promising results have been obtained from basic research. However, clinical data have been limited due to the lack of appropriate implantable stimulators. The major technical hurdle is that the commercially available neuro-stimulators are not adequate for GIES, largely because the gastrointestinal organs are composed of smooth muscles that have a long time constant. That is, much longer pulses are needed to alter functions of the gastrointestinal muscles. Accordingly, most available data in the literature are derived from animals using external stimulators.

Major gastrointestinal disorders that may be treated using electrical stimulation include gastroesophageal reflux, gastroparesis (delayed gastric emptying), intestinal pseudoobstruction, constipation and fecal incontinence. These disorders are mainly attributed to weak sphincter and lack of propulsive contractions along the gut.

Typically, long pulses with pulses width > 50ms are used for electrical stimulation of the gut. It is called long pulse electrical stimulation. Electrical stimulation is delivered via a pair or pairs of stimulation electrodes chronically implanted on gut serosa.

In this presentation, the effects of GIES on lower esophageal sphincter pressure, gastric/intestinal contractions, gastric emptying, small and large intestinal transit and anal sphincter pressure will be introduced. Excitatory GIES on gastrointestinal motility has therapeutic potentials for various gastrointestinal disorders. Basic and clinical data on these potential applications of GIES will be presented.

In addition to the potential applications of GIES for various gastrointestinal disorders, therapeutic potentials of GIES for obesity will also be introduced. Obesity has becoming an epidemic health problem, claiming about 400,000 lives and costing about 100 billions annually in USA alone. However, there is a lack of effective and safe therapy for obesity. Recent clinical studies on the use of GIES for the treatment of obesity will also be introduced in this presentation. Limitations, potentials and possible mechanisms of GIES for the treatment of obesity will be discussed.

Learning Objectives
1. Describe the physiology and pathophysiology of gastrointestinal motility;
2. Explain the basic methodologies of gastric and intestinal electrical stimulation;
3. List potential applications of gastrointestinal electrical stimulation for various disorders of the gut.

1000 – 1030 Break

1030 – 1110 Princesa Ballroom B-C (13)
INS General Assembly
Conference Adjourned