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Chair’s Message

We present the Winter 2010 issue of our departmental newsletter. We are happy to report that another of our faculty, Krishnan Dhandapani, Ph.D., has been awarded a $1.6 million NIH RO1 grant for his proposal evaluating neuroinflammation in traumatic head injury. The first phase of the renovation of our Neuroscience ward culminated in a dedication ceremony in August 2009. Additionally, we are delighted that our $25 million five-year Neuroscience business plan was approved by the administration. This combined Neurology/Neurosurgery business plan will ensure that our goals of maintaining excellence in patient care, teaching and research are met. We thank Mr. Chris Bonham, administrative director of the neuroscience center, for the long hours of work dedicated to this opus. The clinical spotlight this issue is on the continuing tradition of excellence in functional and stereotactic neurosurgery and is authored by Cole Giller, M.D., Ph.D., director of this division. We also document the accomplishments of our faculty and present our academic productivity over the preceding six months. Finally, we acknowledge the generosity of the donors to our department.

Cargill H. Alleyne, Jr., M.D.
Professor and Marshall Allen Distinguished Chair

Department News

3 North renovation completed

The first stage in the renovation of our Neuroscience ward on 3 North was completed in August. The new state-of-the-art ward consists of 16 neurology/neurosurgery private rooms each with a computer with educational information. The ward also includes a family consultation room with computer/DVD/TV, a healing arts program, music therapy, a resource library, and a vending area. 3 West is currently undergoing renovation and an additional ten universal (ICU-general floor care) patient rooms will be completed in May for a total of twenty. The photos above show a patient room (fig 1a), a view from one of the nursing stations (fig 1b), and the ribbon cutting ceremony (fig 1c). Shown in the latter photograph are (from L to R) Roscoe Brown (patient advisor), Don Snell (former CEO of MCG Health), David Hess, M.D. (chair of Neurology), Cargill Alleyne, M.D., Barbara Hines (patient advisor), and Ms. Sandy McVicker (current interim CEO of MCG Health).

NIH RO1 and AHA grants awarded

We congratulate Krishnan Dhandapani, Ph.D. on the award of a $1.6 million, National Institutes of Health RO1 grant for his project entitled: “HMGB1 and traumatic brain injury”. The goal of this study is to determine whether HMGB1 – Toll-like receptor 4 signaling promotes neuroinflammatory activation and cerebral edema after traumatic brain injury.

He was also awarded an American Heart Association (Greater Southeast Affiliate Beginning Grant in Aid) for the project: “Mechanisms of SAH-induced acute brain injury”. The goal of this grant ($132,000) is to determine the potential role of glutamatergic signaling in the progression of acute brain injury following subarachnoid hemorrhage in mice.

Five-year Center of Excellence business plan approved

Under the leadership of our business manager, Chris Bonham, M.B.A., The Neuroscience Center of Excellence five-year strategic plan was presented to the School of Medicine, Board of MCG Health and the Physician’s Practice group in October. This comprehensive $25 million investment includes strategic initiatives in a variety of programs including Stroke, Epilepsy, Gamma knife, General Neurosurgery, General Neurology and Spine surgery. Specific initiatives planned include upgrades to the neuroangiography suite and the gamma knife and recruitment of additional Neurointerventionalists.

Business of Healthcare course initiated

This summer an innovative, one- to two-year business course was begun as part of our educational conference schedule. Delivered by Chris Bonham, M.B.A., Cole Giller, M.D., Ph.D., M.B.A., and Bill Hamilton, M.B.A., M.H.A., the ongoing monthly lectures cover topics such as: Understanding hospitals; Profit vs. non-profit; Negotiation; Hospital/physician relationships; Management and Leadership; Health care economics; Healthcare reform; and Entrepreneurialism.

Contributor acknowledgement

We thank the following donors to our department:

- Carol Moore
- William Pritchard
- A.R.Staulcup foundation
Clinical Spotlight

Physiological and Anatomic Discoveries: Continuing the Tradition of Functional Neurosurgery at MCG

The field of functional neurosurgery addresses some of the most understandable as well as some of the most challenging tasks imaginable in neurosurgery. On the one hand, its goal is simply to alter aberrant function – for example, to remove a seizure focus in order to treat epilepsy, or to inhibit a wayward thalamic nucleus to lessen the symptoms of Parkinson’s disease. On the other hand, the sites of abnormal neurological function are not labeled in nature, and must therefore be discovered during these procedures for each particular patient. Unfortunately, making such discoveries is not automatic – the brain does not willingly yield its secrets – and even a partial answer has always demanded the full technology of the day.

These problems have been faced throughout the nearly five decades of the rich tradition of functional neurosurgery at MCG. Early thalamotomies by Dr. Marcelino Chavez and later by Dr. Marshall Allen in the 1960s relied on ventriculography to discover the correct site for ablation – CT and MRI had not yet been invented! The arrival of Dr. Herman Flanigin in 1981 brought the refined techniques of intraoperative mapping and long-term invasive monitoring, powerful tools used to discover the site of the seizure focus. Under the subsequent guidance of Dr. Joseph Smith, techniques such as MEG, SISCOM, and microelectrode recording have been organized at MCG to effectively discover the sites of neurological malfunction in an increasingly complex and difficult array of conditions.

In this article, two case studies show how these methods continue to be refined and expanded by new technologies to make critical discoveries during functional neurosurgery at MCG. During the discussion, we will explicitly indicate (using blue font) the key discoveries made in the course of treating these patients, underlining our theme that established modalities such as microelectrode recording and invasive monitoring are being augmented with new data from image-guided systems and three-dimensional visualization.

Case 1:

A 37 year old ambidextrous man presented with a history of seizures beginning at the age of 13. The seizures occurred about twice each week, typically at night and in clusters. They began with eye opening, stiffening of the right arm, head and eye turning to the right, and progressed to tonic-clonic convulsions and residual right-sided weakness lasting for hours. His seizures were resistant to medications, including carbamazepine, lamotrigine, phenytoin, topiramate, valproate, oxcarbazepine, phe nobarbitol and lorazepam. Evaluation by the MCG Epilepsy Center included Phase I EEG/video monitoring. Although the predominance of epileptiform discharges arose from the left hemisphere, the pattern of both the interictal and ictal recordings was diffuse and did not provide localizing information. Localization was also not evident from the MRI scan, although a PET scan showed decreased activity in the left temporal lobe. A Wada test showed left language dominance but no lateralization of memory. A SISCOM study (Fig. 1), however, showed focal activity in the left supplementary motor cortex (Discovering the site of neurologic function using radiographic studies).

Review of this data at the multidisciplinary MCG epilepsy conference suggested that the seizure focus was located in the supplementary motor cortex, based on the semiology of the seizures, their occurrence at night, the suggestion of late spread to the motor cortex, and the SISCOM images (Discovering the location of the seizure focus from semiology). However, this deduction remained unproven because neither the EEG nor the imaging data were localizing. Accordingly, a recommendation was made for invasive Phase II monitoring of the left hemisphere with implanted depth electrodes and subdural grids, including coverage of the supplementary motor cortex, the lateral frontal lobe, and the lateral and mesial temporal lobe.

A craniotomy was performed, exposing the sagittal sinus to provide access to the interhemispheric fissure and including a temporal craniectomy for access to the inferior temporal lobe. The location of the supplementary motor cortex was identified with an intraoperative image-guided navigation device (Fig. 2), allowing confirmation of landmarks such as the central sulcus and paracentral lobule (Discovering anatomy from image-guidance). A curved subdural grid was first rolled up and then ‘unfurled’ between the veins within the interhemispheric fissure, much as a model ship is
Clinical Spotlight (continued)

unfurled within a bottle, to access the supplementary motor cortex and adjacent areas on the mesial aspect of the frontal lobe. Grids were also placed over the mesial frontal lobe more anteriorly, the lateral frontal and temporal lobes along the orbital surface of the frontal lobe, and along the basal aspect of the temporal lobe (Figs. 3a-c). In addition, three depth electrodes were inserted with image-guidance (Discovery of best trajectories to targets with image-guidance) through the cortex of the lateral temporal lobe into the amygdala and hippocampus. After the grids were in place, the location of selected grid electrodes in relation to underlying gyri was confirmed and recorded with the Stealth device (Discovery of locations of recording electrodes) to assist with the interpretation of the postoperative recordings. Recordings from these electrodes over the next two weeks showed seizure onset from the supplementary motor cortex, in agreement with the site of activity identified by the SISCOM study. A recommendation for resection of this region was made, and the patient counseled that transient but significant motor and speech deficits often follow removal of the supplementary motor cortex. Plans were made to identify and spare the adjacent motor cortex during the procedure.

During the second craniotomy the interhemispheric electrode was temporarily left in place while the Stealth device was used to verify that the electrodes that were active during the seizures were those in contact with the supplementary motor cortex (Discovery of active electrodes with image-guidance). In addition, bipolar cortical stimulation was used to identify the adjacent motor area as the region producing motor activity when stimulated (Discovery of motor cortex using intraoperative stimulation). This was confirmed to be the same region as the precentral gyrus identified by the Stealth navigation. Relying on these data, the supplementary motor cortex was then removed in a subpial fashion, sparing the adjacent motor cortex (Fig. 4).

The patient had some mild and transient right arm weakness, and was discharged home on the fourth postoperative day. As of this writing two months after his resection, he has had no further seizures.

Case 2:

A 60 year old man with Parkinson’s disease presented with worsening dyskinesias, freezing, and falling despite maximal medical management. Although his symptoms responded transiently to L-Dopa, they would return within an hour and he required multiple doses throughout the day. Other medications were discontinued because of hallucinations and impulsive behavior. Deep brain stimulation (DBS) targeting the subthalamic nucleus was considered to treat his medically intractable symptoms. Neurocognitive screening was obtained to confirm the absence of any dementia that might predict post-operative decline, and implantation of the left and right electrodes were planned on separate days to minimize the risk of cognitive impairment.

The details for implantation of the right subthalamic nucleus will be discussed. Using mild sedation, a Leksell stereotactic frame was attached to the head and imaging acquired (Fig. 5). Inversion recovery MRI sequences were used to best visualize subcortical structures (Discovering subcortical targets with customized MRI imaging), and were imported into a stereotactic planning system (iPlan, BrainLab, Germany) that allowed reconstruction in the AC-PC plane for comparison to various stereotactic atlasses. The subthalamic nucleus was identified in three ways. First, its image could be faintly seen in the axial and sagittal views. Second, its position could be inferred relative to other structures such as the red nucleus and mammillothalamic tract in axial views and the internal capsule and substantia nigra in sagittal views. Finally, a computerized stereotactic atlas was deformed to match the MRI scans to confirm the chosen site (Discovery of target location from relationships to surrounding anatomy). A proposed trajectory was then constructed with the planning system, chosen to avoid both the sulci and the ventricular system (Discovery of safe trajectories with multiplanar reconstructions). The details of this planning process are illustrated in Figs. 6a-e.
Clinical Spotlight (continued)

To correct for small errors induced by subtle deformations of the MRI image or by brain shift, microelectrode recording was used to confirm the location of the subthalamic nucleus during the procedure. Microelectrodes were simultaneously inserted along four tracks – tracks 2 mm lateral, posterior and anterior to the presumed target as well as to the target itself. (Discovery of subcortical targets with microelectrode signals). Signals with high cellularity and background characteristic of the subthalamic nucleus were found along the central track, and to a lesser extent within the posterior track (Fig. 7). Because the lateral track was relatively quiet, it was felt that it traversed the white matter of the internal capsule lateral to the subthalamic nucleus, and that the adjacent central track was therefore located within the lateral portion of the subthalamic nucleus (Fig. 8). A microelectrode was therefore inserted 2 mm medial to the central track, confirming the prediction that the signals corresponding to the subthalamic nucleus would be more robust and found over a longer extent (4 vs. 3.5 mm) than obtained from the central track (Discovery of central targets from microelectrode patterns). This medial track was therefore chosen as the insertion site for the DBS electrode itself (Fig. 9).

The patient was then allowed to become fully awake to ensure that stimulation of the DBS electrode did not produce unwanted side effects. With adequate local anesthesia, light sedation and careful positioning, these procedures involve minimal discomfort and are well tolerated. Stimulation at low voltage produced significant improvements in his left-sided rigidity, improved vocalization, and no changes in mentation or eye movement. Paresthesias were only evoked by very high voltages (Discovery of safe and effective stimulation parameters from macrostimulation). It was felt that the DBS electrode was in good position, and the patient was given more sedation before tunneling the device into position (Fig. 10).

Both the left and right DBS electrodes were programmed in the outpatient clinic, producing an improvement in balance and bradykinesia while at the same time allowing decreased doses of ropinrole and L-Dopa. He is followed in the MCG Movement Disorders Clinic to adjust his electrical parameters while further reducing his medication.

Comments

These cases illustrate the many ‘mini-discoveries’ that have been crucial components of the procedures performed throughout the long history of functional neurosurgery at MCG, and continue to be made with new technologies such as image-guided navigation and three-dimensional imaging. Discovering the seizure focus using semiology and confirming the location of the motor cortex by intraoperative stimulation have been standard tasks of epilepsy surgeons for many years, and are now augmented by image-guidance to locate specific important gyri and to verify the location of monitoring electrodes. Discovery of the location of subcortical targets with stereotactic methods and microelectrode recording has also guided movement disorders surgeons for many years, but is now supplemented by more sensitive MRI sequences allowing direct anatomical targeting and by more robust microelectrode recording allowing routine interpretation of multiple electrodes. The current state-of-the-art is not static, however, and new methods such as optical recording, incorporation of MEG and fMRI, and unforeseen technologies will doubtless expand our repertoire of clinical discoveries in the future.

Cole A. Giller, M.D., Ph.D., M.B.A., F.A.C.S., Shyamal H. Mehta, M.D., Ph.D., Anthony M. Murro, M.D.

The MCG Epilepsy Center has been awarded Level IV status by the NAEC and has treated more than 1200 patients undergoing surgery for medically intractable epilepsy. Neurologists Anthony Murro, M.D. and Yong Park, M.D. have recently been joined by fellow neurologists Suzanne Strickland, M.D. (2008) and Sabina Miranda, M.D. (2009). For more information, or to make a referral, please visit us at www.mcg.edu/neurology or call 706-721-1691.

The MCG Movement Disorders Program is a National Parkinson’s Foundation Center of Excellence and offers comprehensive care for all movement disorders, including deep brain stimulation, interdisciplinary care, clinical trials, and a wide array of outreach and support group meetings. For more information, or to make a referral, please visit us at www.mcg.edu/neurology/specialties/md or call 706-721-2798.
Faculty Update

Accomplishments and recognition

Krishnan M. Dhandapani, Ph.D. served on multiple research study panels including the Department of Defense-CDMRP/Psychological Health & Traumatic Brain Injury Research Program, Concepts Awards #2 Study Panel, the Department of Defense-CDMRP/Psychological Health & Traumatic Brain Injury Research Program Detection, Diagnosis, and Prognosis (DDP) Study Panel and the Defense Medical Research and Development Program (DMRDP) Traumatic Brain Injury Study Panel. He also served as an ad hoc grant reviewer for the United States Army Medical Research and Materiel Command (USAMRMC), the Department of Defense-CDMRP/Psychological Health & Traumatic Brain Injury Research Program, Clinical Interventions Research #1 Study Panel, and the Veterans Administration (VA) - NURC R Special Emphasis Study Panel. See the Department News section for the grants awarded to Dr. Dhandapani.

Sergei Kirov, Ph.D. served on the NIH Special Emphasis Panel on Neurodevelopment and Plasticity. He was also Chair of the session on Early Brain Injury after Subarachnoid Hemorrhage at the 10th International Conference on Cerebral Vasospasm in October 2009 in Chongqing, China.

John R. Vender, M.D. is the institutional PI on a recently approved study entitled: “Multi-center study on the effect of SLV334 in moderate and severe traumatic brain injury”. The objective of this study, sponsored by Solvay Pharmaceuticals, is to evaluate this novel agent in the management of patients with severe traumatic brain injury.

Cargill H. Alleyne, Jr., M.D. was elected Vice-Chair of the Neurology/Neurosurgery section of the National Medical Association at its Las Vegas Meeting in July 2009. He was also the moderator at the Clarence S. Greene, Sr., M.D. Stroke Symposium at the same meeting.

Resident’s/Students’ Corner

Accomplishments and recognition

Melissa Laird (4th year graduate student) won a competitive travel award to attend the 2009 National Neurotrauma Society Annual Meeting in Santa Barbara, CA. She was also awarded an American Heart Association grant ($43,540; Dr. Krishnan Dhandapani, mentor) for the project: “HMGB1-TLR4 signaling and traumatic brain injury”. This is a pre-doctoral fellowship to support her graduate training.

Neuroscience Outlook covers now available as posters

Due to numerous requests, the MCG Department of Neurosurgery has made our eye-catching newsletter covers available as 2’x3’ posters.

“Thumbnails” of our covers are shown below; however, larger images can now be viewed at:

www.mcg.edu/som/neurosurgery/posters

For more information on poster availability and prices, call or e-mail Jamie Motley @

(706)721-3071
jmotley@mcg.edu
Presentations and Publications (July 2009 - December 2009)

Presentations


Vender JR: Face pain. Anesthesia Grand Rounds, Medical College of Georgia, July 2009

Alleyne CH: Subarachnoid hemorrhage and management of unruptured intracranial aneurysms. Neurology Residents Noon Conference, Medical College of Georgia, August 2009

Alleyne CH: Introduction to Neurosurgery. Surgery 5000 lecture series, Medical College of Georgia, August 2009


Alleyne CH: Introduction to Neurosurgery. Surgery 5000 lecture series, Medical College of Georgia, September 2009


Vender JR: Update on Neuromodulation. Southern Pain Society and Emory University Dept of Orthopedics Multidisciplinary Pain Management: Delivering Evidence-Based Effective and Efficient Care, Atlanta, GA, October 2009


Kirov SA: Two-photon microscopy of the focal ischemic stroke reveals that spreading depolarizations are the major cause of the secondary injury to dendrites and dendritic spines. The 10th International Conference on Cerebral Vasospasm, Chongqing, China, October 2009

Choudhri HF, Hughes D, Shellito K, Attia WI: Correction of iatrogenic cervical kyphosis. Congress of Neurological Surgeons, October 2009


Giller CA: Desktop neurosurgical planning: Creation of customized three-dimensional images using standard graphics software. Georgia Neurosurgical Society Meeting, Atlanta, GA, November 2009

Alleyne CH: Introduction to Neurosurgery. Surgery 5000 lecture series, Medical College of Georgia, December 2009

Alleyne CH: What is Neurosurgery? Student National Medical Association lecture, Medical College of Georgia, December 2009


Publications


Bollag RJ, Vender JR, Sharma S: Anaplastic meningioma: Progression from atypical and chordoid morphotype with morphologic spectral variation at recurrence. Neuropathology, September 2009, [E publication]


Conference Schedule (January 2010 - June 2010)

All grand rounds and conferences take place on Friday in the 3 West amphitheater.

Jan 22 9:00 - 10:00 Oral Board Review
10:00 - 11:00 Gamma Knife
11:00 - 12:00 Spine Conference
12:00 - 1:00 Case Conference

Jan 29 NO CONFERENCE

Feb 05 9:00 - 10:00 Radiology
10:00 - 11:00 Anatomy
11:00 - 12:00 Spine Conference
12:00 - 1:00 Case Conference

Feb 12 9:00 - 10:00 Oral Board Review
10:00 - 11:00 Gamma Knife
11:00 - 12:00 Spine Conference
12:00 - 1:00 Case Conference

Feb 19 9:00 - 10:00 Anatomy
10:00 - 11:00 Business of Healthcare
11:00 - 12:00 Spine Conference
12:00 - 1:00 Case Conference

Feb 26 9:00 - 10:00 Journal Club
10:00 - 11:00 Board Review
11:00 - 12:00 Spine Conference
12:00 - 1:00 M&M

Mar 05 9:00 - 10:00 Radiology
10:00 - 11:00 Anatomy
11:00 - 12:00 Spine Conference
12:00 - 1:00 Case Conference

Mar 12 9:00 - 10:00 Oral Board Review
10:00 - 11:00 Gamma Knife
11:00 - 12:00 Spine Conference
12:00 - 1:00 Case Conference

Mar 19 9:00 - 10:00 Anatomy
10:00 - 11:00 Business of Healthcare
11:00 - 12:00 Spine Conference
12:00 - 1:00 Case Conference

Mar 26 9:00 - 10:00 Journal Club
10:00 - 11:00 Board Review
11:00 - 12:00 Spine Conference
12:00 - 1:00 M&M

Apr 02 9:00 - 10:00 Radiology
10:00 - 11:00 Anatomy
11:00 - 12:00 Spine Conference
12:00 - 1:00 Case Conference

Apr 09 9:00 - 10:00 Oral Board Review
10:00 - 11:00 Gamma Knife
11:00 - 12:00 Spine Conference
12:00 - 1:00 Case Conference

Apr 16 9:00 - 10:00 Anatomy
10:00 - 11:00 Business of Healthcare
11:00 - 12:00 Neuro 101: Dr. Hamid Shah
12:00 - 1:00 Fluids & Electrolytes

Apr 23 9:00 - 10:00 Journal Club
10:00 - 11:00 Board Review
11:00 - 12:00 Neuro 101: Dr. Doug Hughes
12:00 - 1:00 Pulmonary Physiology

Apr 30 NO CONFERENCE

May 07 9:00 - 10:00 Radiology
10:00 - 11:00 Anatomy
11:00 - 12:00 Spine Conference
12:00 - 1:00 Case Conference

May 14 9:00 - 10:00 Oral Board Review
10:00 - 11:00 Gamma Knife
11:00 - 12:00 Spine Conference
12:00 - 1:00 Case Conference

May 21 9:00 - 10:00 Anatomy
10:00 - 11:00 Business of Healthcare
11:00 - 12:00 Neuro 101: Dr. Patrick Youssef
12:00 - 1:00 Infectious Diseases

Jun 18 9:00 - 10:00 Anatomy
10:00 - 11:00 Business of Healthcare
11:00 - 12:00 Neuro 101: Dr. Doug Hughes
12:00 - 1:00 Pulmonary Physiology

Jul 25 9:00 - 10:00 Journal Club
10:00 - 11:00 Board Review
11:00 - 12:00 Spine Conference
12:00 - 1:00 M & M Spine Conference

Upcoming Meetings (January 2010 - June 2010)

AANS/CNS Section on Disorders of the Spine & Peripheral Nerves
2/17-20, Orlando, FL

AANS/CNS Section on Cerebrovascular Surgery
2/22-23, San Antonio, TX

International Stroke Conference
2/24-26, San Antonio, TX

Southern Neurosurgical Society
2/24-27, Boca Raton, FL

Comprehensive Stroke Management Update 2010
4/9-11-27, Hilton Head Island, SC

Neurosurgical Society of America
4/11-14, Pebble Beach, CA

American Association of Neurological Surgeons
5/1-5, Philadelphia, PA

Georgia Neurosurgical Society
5/28-30, Amelia Island, FL

Society of Neurological Surgeons
6/19-22, New Haven, CT

Credits

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