Editor-in-Chief’s Message

It has been almost two years since we launched our departmental newsletter, Neuroscience Outlook, in the Summer of 2004. In each issue we have illustrated the rapid metamorphosis of our department and highlighted its clinical and research programs and this issue is no exception. The Human Brain Laboratory is featured in Research Spotlight of this issue and in it we outline the innovative strategies that are used to elucidate the neurobiology and physiology of epilepsy and neurogenesis. In our Faculty Update we provide a glimpse of two recent international excursions in which two of our faculty participated; one in Iraq, and the other in Pakistan. We also congratulate two of our faculty on their recent accomplishments. In Departmental News we feature the visit from Professor Johannes Schramm, the establishment of the online course Healthcare Management 101, and the formation of the Normal Pressure Hydrocephalus Management Group.

Finally, we are extremely grateful for the many donations from the various sources as mentioned in the Departmental News section and the Residents’ and Fellows’ corner. Your generous gifts will help us to maintain our goal of academic excellence. We hope you enjoy this issue.

Cargill H. Alleyne, Jr., M.D.
Associate Professor and Academic Vice-Chair
Residency Program Director
Department of Neurosurgery

Department News

Professor Johannes Schramm Hosted as Visiting Professor

We are honored to have hosted Professor Johannes Schramm as Visiting Professor to our department on October 14, 2005. Professor Schramm and his colleagues at University of Bonn, Germany have established a world-class epilepsy research and treatment center. Professor Schramm (pictured third from the left) discussed “The biological and surgical aspects of tumors associated with long term epilepsy” at our Grand Rounds. He also presented “The spectrum of epilepsy surgery” to the residents.

Normal Pressure Hydrocephalus Services Now Available to Patients

The comprehensive services of the Normal Pressure Hydrocephalus (NPH) Management Group are now available to accurately diagnose and safely treat patients suspected of having NPH. NPH is a syndrome characterized by movement disorder (typically gait apraxia), incontinence and dementia. It is on the rise as the population ages. Although the cause is not known in most cases, some patients with NPH have a history of closed head injury, meningitis or subarachnoid hemorrhage. In all NPH cases, enlarged ventricles are seen in the context of minimal atrophy of the brain.

Because of the difficulty in accurately diagnosing the condition, NPH has often been overlooked. Once diagnosed, NPH also has been dismissed without treatment due to the perceived high risk of neurosurgical intervention. When appropriate, the NPH Management Group places a ventriculo-atrial shunt, which can greatly improve patient function.

For more information, please visit www.treatnph.com or call the NPH Management Group at 706-721-7953.

Healthcare Management 101 Established

Bill Hamilton, MBA/MHA, our MCG Neuroscience administrative director, has created Healthcare Management 101, a Web-based course consisting of seven consecutive audio-visual lectures. The course objectives are to understand core competencies in non-clinical health care business and financing, and to gain baseline knowledge for making healthcare business decisions. Each lecture is synchronized with a Powerpoint slide presentation by Mr. Hamilton. Students must take a pretest to determine their knowledge of the material prior to taking the course. Each lecture is a separate module and is followed by a short quiz. Judy Wright, our editor, assisted with the course design. For more information, please contact Bill Hamilton at:

Tel: (706) 721-4533
E-mail: whamilton@mcg.edu

Recognition of Contributors

We thank the family of Ray Staulcup who donated the sum of $2000 to the Brain Tumor Foundation. We also thank Stryker for their contribution of $12,500 and Medtronic for their contribution of $75,000 to fund the Spine fellowship. Other contributions are noted in the Residents’ Corner.
Research Spotlight

The Human Brain Laboratory

A strategic goal in our department is to foster unique research programs. Our basic philosophy is to develop research programs that can be coupled with clinical programs of strength and excellence within our department. An obvious initial choice was for us to create a new basic research program coupled with our surgical epilepsy program.

The surgical epilepsy program of the Department of Neurosurgery at the Medical College of Georgia has set a historical precedence for clinical excellence under the initial leadership of Dr. Herman Flanagan in the 1980s, and has continued to flourish and grow under the leadership and direction of Dr. Joseph Smith for almost the past twenty years.

The Human Brain Laboratory (HBL) was designed with the intention of providing a rich resource for the study of epilepsy by applying fundamental neurobiological concepts to human epilepsy research. The HBL is directed by Dr. Sergei Kirov with Dr. Mark Lee, and includes research scientist Dr. Julia Fomitcheva, post-doctoral fellow Dr. Vladimir Riazanski, and research assistant Deborah Ard. There are multiple clinical and basic research collaborators on campus. The HBL utilizes human brain tissue removed from patients with intractable epilepsy. We work with both cortical and hippocampal tissue. We have also used normal cortical tissue removed during surgery for brain tumors in several patients. We employ an integrated approach, which combines enhanced-resolution optical imaging techniques, such as two-photon laser scanning microscopy (TPLSM) to study dynamic cellular processes in living human brain cells, and sophisticated electrophysiological techniques, such as whole-cell patch clamp. Other predominant research methods include immunocytochemistry, confocal laser scanning microscopy, electron microscopy, and advanced cell biology techniques. This integrated approach allows us to explore the cellular basis of epileptogenesis, understand the causes of seizures, and determine future treatment strategies.

During a surgical procedure, a section of brain tissue that is part of the planned resection is removed en-bloc with a minimal disturbance of the tissue. We use techniques to ensure that the vascular supply to the tissue is not disrupted until just prior to removing it. For cortical tissue, we perform fast, sharp dissection without any vascular coagulation. For hippocampal tissue, we maintain the vascular pedicle while performing the dissection of the entire hippocampus. The brain tissue is immediately placed in chilled, sterile oxygenated artificial cerebrospinal fluid, and then it is quickly transported to the HBL, which is adjacent to the operating room. The tissue is then sliced to 350-500 um thickness and is prepared for experiments. Our results have documented superior tissue quality and viability and have demonstrated normal ultrastructural components of the neocortex as shown with electron microscopy.

We began working with human brain tissue in the HBL in August 2004. In the first 15 months we have utilized cortical tissue from 34 pediatric patients, including hippocampus in 19 patients. Human epilepsy is not a unitary problem, and a single solution to its many aspects is unlikely. Therefore, we are concentrating our efforts on studying the mechanisms that may contribute to altered network function in the human epileptic brain, such as malformations of cortical development, dendritic or axonal reorganization, the polarity and function of gamma-aminobutyric acid (GABA)-mediated synaptic events, and a pathologic activation of astrocytes.

The role of reelin in epileptogenic cortical malformations. Malformations of Cortical Development (MCD) are increasingly recognized as pathophysiologic substrates of human epilepsy. Presently, more than 30% of patients treated surgically for intractable seizures have some form of MCD. Little is known about the mechanisms of intrinsic hyperexcitability of various cortical malformations. Impaired function of reelin, an important regulator of cortical development, is implicated in the pathology of many diseases associated with altered neuronal connectivity. Whether or not impaired reelin function contributes to cellular abnormality leading to seizures is unknown. In humans, its expression is significantly reduced by the end of gestation period. However, reelin-expressing cells seem to persist in adulthood in epileptic patients with cortical abnormalities. (Fomiticheva, MR Lee, RB Hessier, SA Kirov “Role of reelin in epileptogenic cortical malformations in pediatric patients” The American Epilepsy Society and the American Clinical Neurophysiology Society, Washington DC, Dec. ’05). The altered reelin expression could reflect the initial brain insult that leads to abnormal developmental pattern and required reelin function. These changes could also be the adaptive measure to attenuate seizure-induced brain damage. This remains to be elucidated.
Seizure-dependent dendrite dynamics in human brain. Seizure-induced alterations of dendritic arbors result in a partial deafferentation of pyramidal neurons leading to abnormal connectivity. The vast majority of excitatory synapses in the adult brain occur on dendritic spines. In many disorders the dendritic spine pathology may result from a homeostatic compensatory response of neurons to the altered excitatory input to dendritic spines. Our broad hypothesis is that dendritic spines are organized to dynamically keep an optimal level of synaptic activity between neurons. At the sites of massive discharges, such as during epileptic seizures, spines and their synapses may be rapidly removed from an overly active network when the neuron is at risk of excitotoxicity. Thus, dendritic spines may be maintained dynamically in the course of the disease. Newly proliferated spines may contact aberrant post-synaptic targets and if consolidated can rewire an existing brain circuitry. This process may aid the epileptogenesis. Spines are highly dynamic structures on developing neurons. This instability during synaptogenesis is thought to facilitate the formation of synaptic contacts. Spine dynamics decrease when neurons mature. Mature neurons may respond to acute neuronal injury by replaying the developmental program. Therefore, they may constantly break and form new synapses producing significant alterations in synaptic networks. Availability of human slices from different age groups, particularly from pediatric patients, will make it possible to begin depicting dendritic spine dynamics in human epileptic brain. This will be the first study revealing cellular dynamics of human neurons in slices where the native tissue architecture and in vivo cellular milieu is preserved.

The role of astrocytes and GABAergic signaling in epileptogenic human cortex. GABAergic synaptic transmission inhibits neuronal firing and stops the spread of excitatory glutamatergic activity. However, early during development GABA depolarizes neuronal and acts as an excitatory neurotransmitter. Seizure-induced deafferentation may result in pathological recapitulation of this developmental mechanism contributing to the formation of an epileptic network. A recent electrophysiological study by Cohen and co-authors in 2002 implies the contribution of the excitatory GABA to the interictal-like activity in human subiculum in temporal lobe epilepsy. Whether such a developmental switch in GABA-mediated synaptic transmission in some cells in epileptic human neocortex adds to the pathophysiological network activity remains to be elucidated. In addition, seizure-induced astrogliosis is well documented in the epileptic brain. The role of astrocytes in the pathophysiology of epilepsy is just beginning to emerge. The latest study by Tian and co-workers in 2005 suggests that glutamate release by astrocytes can contribute to epileptic activity in animal models of experimental seizure. Our goal is to explore whether these findings can be translated from animal models to the human epileptic brain.

Neurogenesis in mature human brain. It is well accepted that neuroprogenitor cells exist in mature human brain. In addition, seizures may increase neurogenesis in adult brain, which contributes to aberrant connectivity. Recently, we have successfully isolated stem cells from resected human cortex. Though this project is in its early stages, we have succeeded in culturing "neurospheres", which is a grouping of neuroprogenitor cells. We plan to continue isolating human neuroprogenitor cells for further study. Our goal is to develop a model "whole brain" system by transplanting stem cells into human organotypic brain slices in order to study their proliferation, differentiation, and functional interaction with neuronal networks and glial cells.

Human cortical slices as a real-time model for studying and preventing ischemic injury. As we develop more experience with the HBL, we have realized that we are evolving into a laboratory that uses human brain tissue to provide a translational bridge in basic neuroscience research, as opposed to strictly generating epilepsy research. Human brain slices as a model system can offer a missing link between animal models and patients. We are developing an assay using live human cortical slices to test new and potentially neuroprotective strategies against stroke injury that can be later translated into effective therapies. In addition, we hope to generate new data on the cellular dynamics of human neurons and astrocytes during the onset and recovery of simulated stroke. During stroke, when the blood supply to the brain is blocked, nerve cells become deprived of oxygen and glucose. The immediate consequences include a profound reduction in cellular ATP, membrane depolarization (anoxic depolarization), and a massive release of neurotransmitters. Using human cortical slices, we are investigating anoxic depolarization, and associated neuronal and glial swelling during simulated stroke induced by oxygen-glucose deprivation. Intrinsic optical imaging and TPSM is used to track anoxic depolarization and associated injury in time and space. As a result, we anticipate developing a valuable model for reliable discovery and the preliminary screening of candidate therapeutic drugs for human stroke.

As we move forward with the Human Brain Laboratory, we are finding more opportunities for collaboration with other neuroscientists on campus. We believe that while much of our research focus will be on human epilepsy, we will also move in the direction of becoming more of a "core lab" for neuroscience researchers who desire to work with human brain tissue in order to expand their current research. The HBL is entirely financed by departmental funds. However, we are aggressively pursuing extramural funding sources with current or planned grant submissions for all of the above projects.

Mark R. Lee, M.D., Ph.D. and Sergei A. Kirov, Ph.D.

To learn more about the MCG Human Brain Laboratory, please visit:
www.mcg.edu/son/neurosciences/research.htm
Faculty Update

MCG Neurosurgeon Assists Pakistani Earthquake Victims

In October 2005, a massive earthquake struck Pakistan and India, killing 80,000 and injuring almost as many. In the week after the earthquake’s devastation, Haroon Choudhri, M.D., Director of the Neurosurgery Spine Service, was deluged with pleas for help from the region. Reports of the devastation and injury in the region were verified by his father, also a neurosurgeon, who happened to be visiting Lahore when the earthquake struck. On short notice he assembled a team of personnel including his brother, Asim Choudhri, M.D., a Resident in Radiology from Virginia, Lance Perling, M.D., a Neurosurgery Spine Fellow at MCG, and Bill Loftus, a representative of Stryker Corporation, a maker of surgical instruments and supplies. Both MCG and Stryker generously donated equipment and supplies to the cause.

The team traveled first to Lahore, then to Abbottabad, a city near the epicenter of the quake about 100 miles north of Islamabad. Lahore, a city of about ten million, had received a flood of victims from overwhelmed hospitals close to the epicenter. The victims and their caregivers thankfully accepted the team’s supplies and their surgical knowledge, which the team passed on to the local surgeons. The most complex cases were made more difficult by the need for sophisticated instrumentation, some of which was lacking. In one instance the local toolmakers were able to manufacture a vertical distraction cage needed for a procedure. Dr. Choudhri is planning a second trip to Pakistan early this year to care for more patients.

MCG Neurosurgeon Returns from Iraq

David Floyd, M.D., an assistant professor at MCG returned home earlier last year from his second deployment in the Iraqi war. He spent five months in Baghdad at the Flagship Military Hospital, which cares for more than half of the coalition casualties in the war on terror. Dr. Floyd is a lieutenant-colonel in the U.S. Army. During his most recent deployment he served as Theater Consultant for Neurosurgery as well as Chief of Neurosurgery in Baghdad. The living conditions were reasonable, as he lived in a dormitory-styled room in a fixed facility at a hospital once built for Saddam Hussein’s son. This hospital is located in the green zone of Baghdad and more trauma surgery is performed there than in any center in the U.S. Conditions at the site called for full combat conditions given the threat of roadside bombs, mortars, rockets, and abduction.

Dr. Floyd performed numerous procedures on both coalition and Iraqi troops. The injuries differ from ballistic injuries in the U.S. in that the blast effect from the most common weapon used by insurgents (roadside bombs and suicide bombs) creates a brain injury that is often more diffuse and requires a more radical procedure to relieve the swelling that is created.

During his time in Baghdad Dr. Floyd transported multiple brain casualties to other facilities on helicopters and transport planes. He says that this often made for more excitement than he bargained for because of constant fire from the enemy. The overall experience was rewarding because of the number of lives saved and his commitment to the cause. Needless to say, we are all glad of his safe return.
Accomplishments and Recognition

Kimberly Bingaman, M.D. successfully passed the Neurosurgery Oral Board examinations in November 2005. Congratulations Dr. Bingaman!

Michael Jensen, M.S., our medical illustrator, was awarded the Certificate of Merit award in the animation category in the national medical illustrator competition held at the 60th Annual Conference of the Association of Medical Illustrators in Los Angeles, California in July. His work, "An Introduction to the Corticospinal Tract" was designed to facilitate medical student education in the complexities of the neurological pathways in the course of their basic medical training. Mr. Jensen also received the top-ranked award offered by the Vesalius Trust, the $2000 Alan Cole Scholarship, for his project, "Using an Interactive Program to Understand Neurological Deficits." MCG Chair Emeritus of the Department of Neurology and current president of the American Academy of Neurologists Thomas Swift, M.D. served as Mr. Jensen’s advisor.

Residents' and Fellows' Corner

Residency Program Update

Program Length Changed
Beginning in July 2006, the length of the training program will change to six years after surgical internship rather than the current five years. To facilitate the transition we are matching two residents this year in the upcoming match. The extension in the length of training will lead to an enhanced research experience and will afford us the opportunity to eventually introduce new clinical rotations into the program.

Pre-residency Fellowship Continues
We extend thanks to our first preresidency fellow, Derold Santilus, M.D. who completed his fellowship in December 2005. Our next preresidency fellow is Eric Vernier, M.D. from El Salvador. He begins his fellowship in February 2006.

Contributors to the Resident Education Fund
We thank Dr. Marshall Allen who made a donation of $1000 to the resident education fund. We also thank KLS Martin company who donated $3500 for resident education.

Spine Fellowship News

Lance Perling, M.D. will complete a one-year fellowship in Complex Spine Surgery in March 2006. Craig Chebuhar, M.D. will start as the next Clinical Fellow in April 2006. Dr. Chebuhar is a Board Certified Orthopaedic surgeon who is currently in practice in Atlanta. He has ten years of experience but no fellowship training. The Department of Neurosurgery is also pleased to welcome Dr. Walid Attia, a neurosurgeon from Tokyo, who will also start in April as a Research Fellow in Spine Surgery. In addition to observing surgeries and working in the cadaver lab, Dr. Attia will help us to introduce a new program of formal outcome measures for spine surgery patients. He will participate in several ongoing research projects such as Minimally Invasive Spinal Fusion and Thoracic Thoracicombar Reconstruction using vertical distraction cages.
Presentations

Kirov SA, Andrew RD: CNS neurons resist volume change from osmotic stress but not simulated stokes. IV INMED/TINS meeting, La Ciotat, France, September 2005 (Poster)


Alleyne CH: Management of unruptured intracranial aneurysms: Complication avoidance and pitfalls for the young neurosurgeon. Congress of Neurological Surgeons luncheon seminar, Boston, MA, October 2005


Bingaman KD: Infant heads: Too big, too small, abnormally shaped. Pediatric Grand Rounds, Children’s Medical Center at the Medical College of Georgia, Augusta, GA, October 2005


Davies ML, Kirov SA, Fraser DD, Andrew RD: Studies on whole isolated neocortex and hippocampus from young mice during simulated ischemia. Society for Neuroscience, Washington D.C., November 2005 (Poster)


Publications


# Conference Schedule (February 2006 - July 2006)

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

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### Upcoming Meetings (January - June 2006)

**AANS/CNS Cerebrovascular Section and American Society of Interventional and Therapeutic Neuroradiology**
2/17-20, Orlando, FL

**Southern Neurosurgical Society**
3/2-5, Bermuda

**AANS/CNS Section on Disorders of the Spine & Peripheral Nerves**
3/15-18, Orlando, FL

**American Association of Neurological Surgeons**
4/22-27, San Francisco, CA

**Society of Neurological Surgeons**
5/21 - 23, Durham, NC

**Georgia Neurosurgical Society**
5/28 - 28, Sea Island, GA

### Credits
- **Editor-in-Chief:** Cargill H. Alleyne, Jr., M.D.
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- **Illustration and design:** Michael A. Jansen, M.S.
- ** Contributors:**
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