The 2018 Rush Neuroscience Review
A BEAUTIFUL MIND. Despite receiving the world’s highest honor for dementia research in 2018, David Bennett, MD, isn’t resting on his laurels. He continues his tireless efforts to find ways to prevent and cure Alzheimer’s disease. Read about Bennett’s esteemed career, and the cutting-edge research currently under way at the Rush Alzheimer’s Disease Center, on page 53.
CHAIRPERSONS’ LETTER

NEUROSCIENCES AT RUSH: AT A GLANCE

PRIMARY AND ASSOCIATED FACULTY
Department of Neurological Sciences
Department of Neurological Surgery

RESIDENTS AND FELLOWS
Department of Neurological Sciences
Department of Neurological Surgery

ARTICLES
The MIND Diet: Reducing the Risk of Cognitive Decline in Older Adults
Laurel J. Cherian, MD, MS

Mobile Real-Time Tracking of Acute Stroke Patients and Instant, Secure Interteam Communication: The Join App
Stephan A. Munich, MD; Lee A. Tan, MD; Danilo M. Nogueira, MD; Kiffon M. Keigher, ACNP; Michael Chen, MD; R. Webster Crowley, MD; James J. Conners, MD, MS; Demetrius K. Lopes, MD

Developing a Successful Global Neurology Program
Omar K. Siddiqi, MD, MPH; Merritt Brown, MD; Christine Cooper, MD; Masharip Atadzhanov, MD, PhD; Shabir Lakhi, MBChB, MMed, MPH; Igor J. Koralnik, MD

A Rush Resident’s Zambian Experience
Teresa M. Lee, MD

Cortical Stimulation Parameters for Functional Mapping
Jacquelyn A. Corley, MD; Pouya Nazari, MD; Vincent J. Rossi, MD; Nora C. Kim, MD; Louis F. Fogg, PhD; Thomas J. Hoeppner, PhD; Travis R. Stoub, PhD; Richard W. Byrne, MD

Rush Epilepsy Center: A Well-Rooted Tradition of Excellence Branching Out to the Future
Rebecca O’Dwyer, MD; Marvin A. Rossi, MD, PhD; Andrea Bermeo-Ovalle, MD

Cervical Spine Deformity—Part 1: Biomechanics, Radiographic Parameters, and Classification
Lee A. Tan, MD; K. Daniel Riew, MD; Vincent C. Traynelis, MD

RESEARCH GRANTS

VOLUME AND QUALITY DATA
Volumes, neurology and neurological surgery
Mortality, neurology and neurological surgery
Quality indicators, stroke

CHANGING MINDS
Like many people, David Bennett, MD, is concerned about Alzheimer’s disease. Unlike most people, Bennett, director of the Rush Alzheimer’s Disease Research Center and one of the world’s foremost Alzheimer’s researchers, may someday be able to stop it.
Chairpersons’ Letter

At Rush, we embrace diversity, whether it be of thought, of culture and experience, or diversity of expertise. Yet, while each member of the Rush neurosciences team possesses unique talents and perspectives, we all share one belief: A belief in excellence.

This passion for excellence—this desire to push ourselves to do more—revolves around doing what’s right for the people we care for, whether that’s at the bedside, or in the operating room, clinic, or research lab. And this commitment extends not just to Chicago, Oak Park, and Aurora—our primary service areas—but throughout Illinois and even the far reaches of Africa.

Rush’s dedication to excellence can be seen in the quality care it delivers and the outcomes it achieves. National organizations have recognized this commitment through various honors. For example, Vizient, a health services company, consistently ranks Rush among the top 5 academic medical centers in its annual quality and accountability study.

In addition, in 2018 U.S. News & World Report ranked 7 specialty care programs at Rush University Medical Center among the best in the country. We’re proud to say that Rush’s neurology and neurosurgery program is ranked 11th in the country.

To achieve excellence in the neurosciences, we turn to the many talented and highly skilled physicians, researchers, nurses, and allied health professionals on our teams. Their relentless energy and unlimited vision make the impossible possible as they work to find better ways to care for patients.

They reach outside of Rush to share their neurological expertise with other health care professionals as well as help underserved communities. They achieve this through innovative uses of technology, hosting educational symposiums, conducting and publishing relevant research (p. 46), and participating in residency training programs, such as those found at John H. Stroger, Jr. Hospital of Cook County and the University Teaching Hospital in Lusaka, Zambia (see p. 22). In doing so, they bring excellence to many, many others.

The following selected highlights from the past year showcase our faculty’s commitment to excellence at Rush and beyond.

Exploring the power of Aspirin for Alzheimer’s disease:
Researcher Kalipada Pahan, PhD, a professor of neurological sciences, biochemistry, and pharmacology at Rush, and others conducted a study on the effects of a low-dose aspirin regimen in reducing plaques in the brain. In this NIH-funded study, they found that aspirin decreases amyloid plaque pathology in mice by stimulating lysosomes—the component of animal cells that helps clear cellular debris.

The first use of microburst nerve stimulation for drug-resistant epilepsy: Rush was the first health care provider in the world to use microburst vagus nerve stimulation to help patients with epilepsy who are resistant to drug therapy. Neurologist Rebecca O’Dwyer, MD, is currently evaluating the safety and effectiveness of this technique in a clinical trial.

Investigating the link between Alzheimer’s disease and higher blood pressure: In a study published in the online version of Neurology, neurologist Zoe Arvanitakis, MD, and others found a connection between higher blood pressure and an increased number of markers of Alzheimer’s disease in the brain.

A novel method for virus detection in clinical samples: Igor Koralnik, MD, and colleagues developed a novel approach called ViroFind to perform deep nucleotide sequencing to find viruses. It uses probes in a hybridization reaction to enrich viral sequences and enhance the detection of viral genomes via deep sequencing.

Providing specialized epilepsy care to rural communities:
The Rush Epilepsy Center, in collaboration with the Epilepsy Foundation of North Central Illinois, co-founded an innovative population health rural ambulatory care program called The Northern Illinois Rural Population Health Initiative. It delivers mobile, specialized health care to children and adults with medically intractable epilepsy and co-morbid mental health disorders in rural communities. Led at Rush by Marvin Rossi, MD, PhD, the initiative enables epileptologists to use portable communication technologies to provide specialized care for refractory patients in areas that lack this level of medical expertise.

High-density EEG for epilepsy and Progressive Multifocal Leukoencephalopathy (PML): Neurologist Adriana Bermeo-Ovalle, MD, is using high-density EEG combined with high-quality imaging to provide individual mapping of the origins of electrical activity in the brain. This technology is used in the planning of epilepsy surgery but can also become a tool for understanding brain activity in other diseases. Rush is currently looking at the short- and long-term effects of JC virus in the brain of patients with PML using this technology.

Physicians honored for excellence: David Bennett, MD, director of the Rush Alzheimer’s Disease Center, received the highest honor in the world for dementia research from the Academy of Neurology and the American Brain Association: the Potamkin Prize.
Leadership roles in national organizations: Participating in national professional organizations is an important tool in continually improving our areas of specialization. We both have held leadership roles in such organizations, with Richard Byrne, MD, completing his term as president of the Neurosurgery Society of America in 2018, and Igor Koralnik, MD, currently serving as president of the International Society for NeuroVirology. Other members of the neurosciences team currently in leadership roles include Christopher Goetz, MD, who is president of the International Parkinson and Movement Disorders Society.

Strengthening academic ties and caring for the underserved: The neurosurgery and neurology departments continue to strengthen their affiliation with John H. Stroger, Jr. Hospital of Cook County. Rush is the primary academic partner of Stroger’s Division of Neurosurgery, a partnership designed to enhance the collaboration between our departments over the next few years. In the spirit of the larger institutional Rush/Stroger academic affiliation, we plan to offer more subspecialty clinical services and improve the educational experience for neurosurgery residents. In addition, this past year, neurologists from Rush are also serving the needs of underserved populations at Stroger.

High volumes continue in neurosurgery: The last few years have marked the busiest years in our neurosurgery program’s history. We currently have the largest volume for nonspine neurosurgeries in the 8-county region for the 8th straight year.* This has been largely fueled by additional dedicated academic faculty, and the growth of programs in vascular neurosurgery and brain tumor surgery. Although we are pleased by the growth in volume, our primary focus will always be quality. University Health Consortium has routinely placed some of our programs among the nation’s top performers in terms of outcomes. For more on quality and volumes, see pages 51-52.

We encourage you to read more about the contributions of the neuroscience program at Rush in this year’s Rush Neuroscience Review. In sharing our work with you, we celebrate our program’s excellence and achievements, but we also hope that the discoveries and stories in these pages will inform and inspire.

Richard Byrne, MD
Chairperson, Department of Neurological Surgery
The Roger C. Bone, MD, Presidential Chair

Igor Koralnik, MD
Chairperson, Department of Neurological Sciences
The Jean Schweppie Armour Professor of Neurology

*Based on data as of third quarter of FY18.
Neurosciences at Rush: At a Glance

Department of Neurological Sciences
- Rush Alzheimer’s Disease Center
- Section of Cerebrovascular Disease
- Section of Clinical Neurophysiology and Epilepsy
- Section of Cognitive Neurosciences
- Section of Critical Care Neurology
- Section of General Neurology
- Section of Movement Disorders
- Rush Multiple Sclerosis Center
- Section of Neuroinfectious Diseases
- Section of Pediatric Neurology
- Section of Neuromuscular Diseases
- Section of Neuro-oncology
- Section of Neuro-ophthalmology

Department of Neurological Surgery
- Neuroendovascular Surgery Center
- Skull Base and Pituitary Surgery Center
- Spine and Back Care

For additional volume and quality data, see pages 51-52.

Neurology outpatient visits 32,539
Neurology inpatient discharges 2,538
Neurological surgery outpatient visits (brain) 4,334
Neurological surgery outpatient visits (spine) 6,498

Attending physicians 126
Residents and fellows 58
Advanced practice nurses and physician assistants 33

Inpatient Facilities

<table>
<thead>
<tr>
<th>Beds</th>
<th>General neurology</th>
<th>Neurosurgery</th>
<th>Neuro ICU</th>
<th>Psychiatric</th>
<th>Rehabilitation</th>
<th>Epilepsy (adult)</th>
</tr>
</thead>
<tbody>
<tr>
<td>32</td>
<td>28</td>
<td>28</td>
<td>67</td>
<td>54</td>
<td>10</td>
<td></td>
</tr>
</tbody>
</table>
Rett Syndrome Clinical Research Center of Excellence: The Rush Rett Multidisciplinary Clinic was designated as a Rett Syndrome Clinical Research Center of Excellence by Rettsyndrome.org (formerly the International Rett Syndrome Foundation). Rush is one of only 14 centers nationwide, and the only one in Illinois, to earn this distinction.

No. 11 in the Nation: The Neurology and Neurosurgery Program at Rush is ranked No. 11 in the nation by U.S. News & World Report.

Mobile Stroke Unit: In 2018, Rush’s Mobile Stroke Unit began serving patients in Chicago’s near west suburbs. This state-of-the-art ambulance—equipped with a team of emergency stroke care specialists, imaging, telemedicine technology, and clot-busting medications—enables stroke patients to be treated on-site instead of having to wait until they get to the hospital.

Level 4 Epilepsy Center: The Rush Epilepsy Center has been accredited as a Level 4 Epilepsy Center by the National Association of Epilepsy Centers for providing a comprehensive approach to the diagnosis and treatment of epilepsy.

MS Comprehensive Care Center: The National MS Society’s Partners in Care Program has recognized Rush as a Center for Comprehensive Care, recognition of Rush’s excellence in MS treatment and research.

Lewy Body Dementia Research Center of Excellence: Rush is the only center in Illinois and one of only 33 centers nationwide to be named a Research Center of Excellence by the Lewy Body Dementia Association (LBDA).
**Faculty (2018)**

Department of Neurological Sciences

**Chairperson:** Igor Koralnik, MD

### Aging and neurodegenerative diseases
- Neelum Aggarwal, MD
- Zoe Arvanitakis, MD, MS
- Lisa Barnes, PhD
- David Bennett, MD
- Katherine Blizinsky, PhD
- Aron Buchman, MD
- Ana Capuano, PhD
- Phil De Jager, MD, PhD
- Debra Fleischman, PhD
- Chris Gaiteri, PhD
- Duke Han, PhD
- Namhee Kim, PhD
- Sue Leurgans, PhD
- Julie A. Schneider, MD
- Yanling Wang, PhD
- Robert Wilson, PhD
- Lei Yu, PhD

### Cerebrovascular disease
- James Conners, MD, MS
- Laurel Cherian, MD, MS
- Rima Dafer, MD, MPH, FAHA
- Nick Osteraas, MD
- Sarah Song, MD, MPH
- Alejandro Vargas, MD MS

### Clinical neurophysiology and epilepsy
- Antoaneta Balabanov, MD
- Adriana Bermeo-Ovalle, MD
- Lawrence Bernstein, MD
- Thomas Bleck, MD
- Maggie McNulty, MD
- Rebecca O'Dwyer, MD
- Marvin Rossi, MD, PhD
- Michael Smith, MD

### Critical care neurology
- Thomas Bleck, MD
- Torrey Boland Birch, MD
- Michael Chen, MD
- Ivan DaSilva, MD
- Rajeev Garg, MD, MS
- Sayona John, MD
- Lauren Koffman, DO
- George Lopez, MD, PhD
- Sebastian Pollandt, MD
- Starane Shepherd, MD

### Cognitive neurosciences
- Christopher Grote, PhD
- Duke Han, PhD
- Richard Peach, PhD
- Robert Wilson, PhD

### General neurology
- Amar Bhatt, MD
- Iulia Dorneau, MD
- Andrew Dorsch, MD
- Jacob Fox, MD
- Laura Goldstein, MD
- Christopher Muth, MD
- Malathi Rao, MD
- Ligia Rioja, MD
- Megan Shanks, MD
- Milena Stosic, MD
- Aimee Szewka, MD
- Jessica Wilson, MD
- Robert Wright, MD

### Multiple sclerosis
- Michael Ko, MD
- Thomas Shoemaker, MD
- Fabian Sierra-Morales, MD
- Dusan Stefoski, MD

### Neurobiology
- Yaping Chu, PhD
- Xin Dang, PhD
- Malabendu Jana, PhD
- Jeffrey Kordower, PhD
- Susanta Mondal, PhD
- Dan Nicholson, PhD
- Kalipada Pahan, PhD
- Avik Roy, PhD
Neuroinfectious diseases
Igor Koralnik, MD
Fabian Sierra-Morales, MD

Neuromuscular diseases
Ryan Jacobson, MD
Peter T. Heydemann, MD
Rabia Malik, MD
Irwin Siegel, MD
Madhu Soni, MD

Neuro-oncology
Joo Yeon Nam, MD
Clement Pillainayagam, MD

Neuro-ophthalmology
Milena Stosic, MD
Aimee Szewka, MD

Parkinson's disease and movement disorders
Mitra Afshari, MD
Sharlet Anderson, PhD
Meagan Bailey, MD
Brandon Barton, MD, MS
Bryan Bernard, PhD
Cynthia Comella, MD
Melany Danehy, MD
Jori Fleisher, MD, MSCE
Christopher Goetz, MD
Deborah A. Hall, MD, PhD
Aikaterini Kompoliti, MD
Bichun Ouyang, PhD
Gian Pal, MD, MS
Glenn Stebbins, PhD
Leonard Verhagen Metman, MD, PhD

Pediatric neurology
Elizabeth Berry-Kravis, MD
Colleen Buhrfriend, MD
Peter Heydemann, MD
Charles Marcuccilli, MD
Lubov Roman'tseva, MD

Department of Neurological Surgery

Chairperson: Richard Byrne, MD
Richard Byrne, MD
Michael Chen, MD
R. Webster Crowley, MD
Harel Deutsch, MD
Richard Fessler, MD, PhD
Ricardo Fontes, MD, PhD
Lorenzo Munoz, MD
John O'Toole, MD, MS
Sepehr Sani, MD
Vincent Traynelis, MD

Research faculty
Brian David, PhD
Gele Liu, PhD
Roberta Glick, MD
Richard Penn, MD

Associated faculty at Rush University Medical Center
Pete Batra, MD – Otorhinolaryngology
Adnag Diaz, MD, MPH – Radiation oncology
Sheila Dugan, MD – Physical medicine and rehabilitation
John Furrey, MD – Physical medicine and rehabilitation
David Rothenberg, MD – Anesthesiology
Mary Sturaitis, MD – Anesthesiology
R. Mark Wiet, MD – Neurotology

Associated clinical faculty*
Bryan Bertoglio, MD
Tibor Boco, MD
George Bovis, MD
Fady Charbel, MD
Egon Doppenberg, MD
Juan Jimenez, MD
Dean Karahalios, MD
Kevin Kelly, MD
Shaun O'Leary, MD
Demetrius Lopes, MD
Martin Luken, MD
Patricia Raskin, MD
Szymon Rosenblatt, MD
Dmitry Ruban, MD
John Ruge, MD
Andrew Zelby, MD

*Primary appointment is not at Rush University Medical Center

Faculty (2018) 7
Residents and Fellows (2018)

Department of Neurological Sciences

Residents

Nandini Abburi, MD
Medical school: University of Toledo, College of Medicine

Hannah Breit, MD
Medical school: Wake Forest University School Of Medicine

Catherine Daley, MD
Medical school: University of Toledo College of Medicine

Gregory Fenton, MD
Medical school: Boston University School of Medicine

Rachel Forman, MD
Medical school: Rosalind Franklin University Of Medicine & Science/Chicago Medical School

Edie Graham, MD
Medical school: Loyola University of Chicago, Stritch School of Medicine

Christopher Green, MD
Medical school: Rush Medical College

Emily Grodinsky, MD
Medical school: Cornell University, JS Weill Medical College

Heather Heiser, MD
Medical school: Michigan State University, College of Human Medicine

Teresa Lee, MD
Medical school: Georgetown University School of Medicine

Stephanie Lyden, MD
Medical school: University of Washington School of Medicine

Fiona Lynch, MD
Medical school: Rush Medical College

Jacob Manske, MD
Medical school: Rush Medical College

Allie Osen, MD
Medical school: Indiana University, School of Medicine

Sunny Qiu, MD
Medical school: Duke University School of Medicine

Jeffrey Quinn, MD
Medical school: Loyola University of Chicago, Stritch School of Medicine

Lauren Singer, MD
Medical school: Oakland University, William Beaumont School Of Medicine

Kathy Slota, MD
Medical school: Rosalind Franklin University Of Medicine & Science/Chicago Medical School

Tammy Smith, MD
Medical school: University of Utah School of Medicine

David Smyth, MD
Medical school: University of Utah, School of Medicine

Maggie Stepien, MD
Medical school: Rush Medical College

Andrea Sterenstien, MD
Medical school: Rosalind Franklin University Of Medicine & Science/Chicago Medical School

Jake Torrison, MD
Medical school: University of North Dakota School of Medicine

David Walker, MD
Medical school: Rush Medical College

Fellows

Fawaz Ahmad, MD
Medical school: University of Arkansas, College of Medicine
Residency: Greater Baltimore Medical Center

Zeeshan Ali, MD
Medical school: Indiana University School of Medicine
Residency: Rush University Medical Center

Izabela Biesiada, DO
Medical school: West Virginia School of Osteopathic Medicine
Residency: University of Illinois at Chicago

Hunan Chaudhry, MD
Medical school: Rush Medical College
Residency: Rush University Medical Center

Christine Chuck, MD
Medical school: Indiana University School of Medicine
Residency: Rush University Medical Center

Sarah Corbridge, MD
Medical school: Ben-Gurion University of the Negev
Residency: University of Wisconsin SOM and Public Health

Chandler Gill, MD
Medical school: Loyola University of Chicago, Stritch School of Medicine
Residency: Loyola University Medical Center

Anjali Gera, MD
Medical school: University of Illinois at Chicago, College of Medicine
Residency: University of Chicago

Ryan Hanson, MD
Medical school: Rush Medical College
Residency: Rush University Medical Center

Alana Kirby, MD
Medical school: University of Michigan Medical School
Residency: Beth Israel Deaconess Medical Center/ Harvard Medical School

Wajahat Lodhi, MBBS
Medical school: NTR University
Residency: Fairview Hospital, Cleveland Clinic
Department of Neurological Surgery

Residents

Alok Patel
Medical school: Ross University
Residency: Cooper University Hospital

Gopi Patel, MD
Medical school: Tianjin Medical University
Residency: University of Illinois in Peoria

Stasia Rouse, MBchB
Medical school: University of Pretoria
Residency: Johannesburg General

Rasha Waheed, MD
Medical school: University of Baghdad
Residency: Baghdad Teaching Hospital

Natalie Witek, MD
Medical school: Boston University School of Medicine
Residency: University of California, San Francisco

Shahjehan Ahmad, MD
Medical school: University of Arizona College of Medicine

Adewale Bakare, MD
Medical school: Indiana University School of Medicine

Andre Beer Furlan, MD
Medical school: University of Sao Paolo

Bledi Brahimaj, MD
Medical school: University of Cincinnati College of Medicine

Daniel Eddelman, MD
Medical school: Indiana University School of Medicine

David Fessler, MD, PhD
Medical school: University of Cincinnati, College of Medicine

Mena Kerolus, MD
Medical school: University of Missouri-Kansas City Combined BA/MD Program

Ryan Khanna, MD
Medical school: Northwestern University Feinberg School of Medicine

Ryan Kochanski, MD
Medical school: Wayne State University School of Medicine

Joseph Molenda, MD
Medical school: Johns Hopkins School of Medicine

Joseph Morrison, MD
Medical school: University of Illinois College of Medicine

Ravi Nunna, MD
Medical school: University of Cincinnati College of Medicine

John Pearce, MD
Medical school: Lewis Katz School of Medicine

Andrew Wong, MD
Medical school: Jacobs School of Medicine and Biomedical Sciences at the University at Buffalo

Joshua Woodward, MD
Medical school: Oregon Health Sciences School of Medicine

Fellows

Hormuz Dasenbrock, MD
Medical School: Johns Hopkins University School of Medicine, Residency: Brigham & Women's Hospital, Boston Children's Hospital, & Harvard Medical School

Anan Shwete, MD
Medical School: Hadassah Medical School at the Hebrew University
Residency: Sheba Medical Center

Christopher Witw, MD
Medical school: University of Manitoba, Faculty of Medicine
Residency: University of Toronto
THE MIND DIET:
Reducing the Risk of Cognitive Decline in Older Adults

Laurel J. Cherian, MD, MS

Author Affiliation: Department of Neurological Sciences, Rush University Medical Center, Chicago, Illinois
Corresponding Author: Laurel J. Cherian, MD, MS, Department of Neurological Sciences, Rush University Medical Center, Chicago, IL 60612 (laurel_j_cherian@rush.edu).

Introduction

The Rush Stroke Program, Rush Institute for Healthy Aging, and Rush Alzheimer’s Disease Center are known for excellent clinical work and research. These programs have combined forces to produce exciting research that provides new insights into the role nutrition plays in maintaining cognition and mental health in older adults, including those who have experienced a stroke. While the risks of cognitive decline and depression are concerns for all adults as they age, stroke survivors are at exceptionally high risk, with a rate of dementia as high as double that of the general population.

To understand how lifestyle factors may decrease the risk of cognitive decline in older adults with a history of stroke, Laurel Cherian, MD, MS, Neelum Aggarwal, MD, and Martha Clare Morris, ScD, focused on nutrition and specific dietary patterns in older adults.

The MIND (Mediterranean-DASH Intervention for Neurodegenerative Delay) diet, created by Dr Morris, was based on years of research on the foods and nutrients that influence brain health. Components of the MIND diet include whole grains, green leafy vegetables and other vegetables, berries, beans, nuts, fish, poultry, wine, and olive oil, with limited consumption of red meat and red-meat products, whole-fat cheese, fried food/fast food, butter, and sweets and pastries (Figure 1).

In 2015, a publication in the journal Alzheimer's and Dementia reported that the MIND diet slowed cognitive decline in a

The MIND Diet

**Recommended:**
- Whole grains, ≥3 servings per day
- Green leafy vegetables, ≥6 servings per week
- Other vegetables, ≥1 servings per day
- Berries, ≥2 servings per week
- Fish, ≥1 servings per week
- Poultry, ≥2 servings per week
- Beans, >3 servings per week
- Nuts, ≥5 servings per week
- Primary use of olive oil
- Alcohol/wine, 1 serving per day

**Discouraged:**
- Red meat and red-meat products, <4 servings per week
- Fast food/fried food, <1 serving per week
- Butter/margarine, <1 teaspoon per day
- Cheese, <1 serving per week
- Pastries/sweets, <5 servings per week

Figure 1. The MIND diet.
community population of older adults participating in the Memory and Aging Project, but it was not known whether the diet would also be effective in stroke survivors.

The Rush Memory and Aging Project (MAP) was initiated more than 20 years ago by David Bennett, MD, recent winner of the Potamkin Prize for Research in Pick’s, Alzheimer’s, and Related Diseases awarded by the American Academy of Neurology and the American Brain Foundation (see interview with Dr Bennett on page 53). MAP participants are recruited from retirement communities in the Chicago area. They must be free of dementia at enrollment, agree to annual comprehensive examinations that include a series of 19 cognitive tests, and agree to brain donation at death.

Methods

MIND Diet and Cognitive Decline in Stroke Survivors

Drs Cherian, Aggarwal, and Morris identified 108 MAP participants who had a history of stroke, nutrient data from a food frequency questionnaire, and cognitive test scores. MIND diet scores were computed from responses to questions about the frequency of consumption of 144 food items from the food frequency questionnaire. Change in global cognitive scores over an average of 4.7 years was regressed on baseline MIND score and modeled in tertiles, using linear mixed models.

Results showed that higher adherence to the MIND diet was associated with a substantially slower rate of cognitive decline (β = 0.08; P = .03 for tertile 3 vs tertile 1) with adjustment for age, sex, education, presence of the apo-E4 gene, late-life cognitive activity, caloric intake, physical activity, and smoking (Figure 2).

The study was presented at the American Heart Association’s International Stroke Conference in January 2018 and the American Academy of Neurology’s Annual meeting in April 2018. The abstract was also covered extensively in the press, including stories on ABC news and in The Independent.

Effects of Diet on Depressive Symptoms in Older Adults

Drs Cherian, Aggarwal, and Morris then turned their attention to the role that diet may have in reducing depressive symptoms in older adults, as prior studies have suggested that nonpharmacologic strategies to reduce depression, such as diet, may be effective. In this second study, a total of 964 MAP participants were assessed annually for depressive symptoms over an average of 6.5 years of follow-up using a 10-item version of the Center for Epidemiologic Studies Depression scale. Depression was defined as the presence of 4 or more depressive symptoms. Diet scores were computed from the dietary questionnaire for the DASH (Dietary Approaches to Stop Hypertension), Mediterranean, MIND, prudent, and Western diets and modeled in tertiles. A generalized estimating equation model was used to perform the longitudinal analysis of depression as a binary outcome adjusted for age, sex, education, late-life cognitive activity, physical activity, diabetes, hypertension, stroke, and myocardial infarction.

The MIND and DASH diet scores were associated with lower risk of developing depressive symptoms, and the Western diet score was associated with greater risk (for tertile 3 vs tertile 1: DASH, β = −0.11, P < .01; MIND, β = −0.08, P = .01; Western, β = 0.02, P = .04), suggesting that diet modification may be effective in preventing depression (Table).

This study was presented at the American Academy of Neurology’s annual meeting in Los Angeles in April 2018. Media coverage of this study has included pieces aired on National Public Radio and Good Morning America and articles published in The Wall Street Journal, The Telegraph, and USA Today.

Diet Patterns and Brain Neuropathology

Lastly, Drs Aggarwal, Cherian, and Morris turned their attention to the role of diet patterns to brain neuropathology in 468 MAP participants who died over the course of the study and donated their brains. This study, which was presented at the Alzheimer’s Association International Conference (July 22-26, 2018), found that a Western-style diet was related to increased Alzheimer’s disease neuropathology and vascular neuropathology.
Autopsied brains were analyzed in multiple brain regions for β-amyloid plaques and tau tangle density, neocortical Lewy bodies, hippocampal sclerosis, gross and microscopic cerebral infarcts, cerebral atherosclerosis and arteriosclerosis, and summary measures computed based on published criteria for the NIA-Reagan (National Institute of Aging–Reagan Institute) Alzheimer’s disease neuropathology diagnostic score (low, intermediate, or high pathology), Braak stage (neurofibrillary tangle stage I to VI), and CERAD (Consortium to Establish a Registry for Alzheimer’s Disease) score (neuritic plaque severity). In analytic models adjusted for age, sex, and education, higher Western diet scores were significantly associated with greater neuritic plaque severity ($\beta = 0.33$, $P = .01$), higher amyloid level ($\beta = 0.64$, $P = .01$), higher NIA-Reagan score ($\beta = 0.16$, $P = .05$), and greater probability of arteriolosclerosis (odds ratio, 1.31; 95% CI, 1.04 to 1.64).

### Conclusion
These studies were supported by multiple grants from the National Institute on Aging, and the results will form the basis for a proposed clinical trial to investigate the effectiveness of the MIND diet intervention to reduce cognitive decline and depressive symptoms in stroke survivors. One novel element of the proposed trial is the use of a meal delivery service, helping to eliminate the burden of shopping and food preparation for stroke survivors and/or their caregivers and to provide easy, consistent access to high-quality nutrients during the critical early months after a stroke. We are excited to combine the strengths of the Rush Stroke Program, Institute for Healthy Aging, and Alzheimer’s Disease Center to provide the best care and cutting-edge research for our patients.

### Table. Incidence of Depression Over Time by Dietary Pattern

<table>
<thead>
<tr>
<th>Dietary Pattern</th>
<th>Depression Incidence, $\beta$ (95% CI) (n = 867)</th>
<th>Linear Trend</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dash Diet</strong></td>
<td></td>
<td></td>
<td>.002$^b$</td>
</tr>
<tr>
<td>Tertile 1</td>
<td>Reference</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tertile 2</td>
<td>$-0.089 (-0.16, -0.014)$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tertile 3</td>
<td>$0.12 (-0.20, 0.034)$</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Mediterranean Diet</strong></td>
<td></td>
<td></td>
<td>.23</td>
</tr>
<tr>
<td>Tertile 1</td>
<td>Reference</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tertile 2</td>
<td>$0.003 (-0.063, 0.068)$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tertile 3</td>
<td>$0.062 (-0.15, 0.025)$</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>MIND Diet</strong></td>
<td></td>
<td></td>
<td>.076</td>
</tr>
<tr>
<td>Tertile 1</td>
<td>Reference</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tertile 2</td>
<td>$0.014 (-0.062, 0.090)$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tertile 3</td>
<td>$-0.077 (-0.15, -0.002)$</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

---

$^a$ Adjustments were made for age, sex, education, late-life cognitive activity, physical activity, diabetes, hypertension, stroke, and myocardial infarction.

$^b$ Statistically significant as determined by 95% CI and $P < .05$. 

* Conclusion

These studies were supported by multiple grants from the National Institute on Aging, and the results will form the basis for a proposed clinical trial to investigate the effectiveness of the MIND diet intervention to reduce cognitive decline and depressive symptoms in stroke survivors. One novel element of the proposed trial is the use of a meal delivery service, helping to eliminate the burden of shopping and food preparation for stroke survivors and/or their caregivers and to provide easy, consistent access to high-quality nutrients during the critical early months after a stroke. We are excited to combine the strengths of the Rush Stroke Program, Institute for Healthy Aging, and Alzheimer’s Disease Center to provide the best care and cutting-edge research for our patients. *
Introduction

Technologic advances in therapeutic strategies for the treatment of ischemic conditions, such as myocardial infarction and ischemic stroke, have markedly improved outcomes. However, advancement and development of the infrastructure housing these therapeutic approaches are critical, yet often overlooked, components of providing optimal care for patients suffering these conditions. To address this need, our institution has designed and implemented a multidisciplinary and multi-institutional workflow and infrastructure to support and streamline the treatment of patients with acute ischemic stroke. One novel component of this process is our implementation of a mobile smartphone software application that allows patient tracking and secure communication among treatment team members.

More than two-thirds of physicians regularly use smartphones. Mobile smartphone applications are being used broadly in neurological disease management, spanning from disease prevention to tracking of long-term follow-up. Mobile applications have been utilized in a variety of ways for the management of acute ischemic stroke: digital health interventions for the reduction of vascular risk factors and prevention of cardiovascular diseases, diagnosis of stroke at telestroke centers, calculation of National Institutes of Health Stroke Scale (NIHSS) and ASPECT (Alberta Stroke Program Early CT) scores, and automated assessment of the modified Rankin scale after discharge. The utilization of mobile smartphone technology in the triage and management of patients with acute ischemic stroke may further streamline management of these patients. Here, we describe our experience implementing the Join smartphone application (Allm Inc, Tokyo, Japan) at our comprehensive stroke center. We aim to describe the impact of the application on our workflow and report the impressions of our team in implementing this application.

Materials and Methods

Clinical Workflow for Acute Ischemic Stroke Triage and Management

Our “Stroke 60” acute ischemic stroke workflow typically begins with a call from an outside facility where there is a patient in whom ischemic stroke is suspected (Figure 1). The stroke neurologist at our institution discusses the patient and reviews available imaging. The neurologist discusses the case with the neurointerventionalist, and the decision to transfer the patient for endovascular intervention is made. If the patient meets criteria for intravenous thrombolytics, this treatment is typically administered at the outside facility and continued during transport (ie, “drip and ship” model). Upon an affirmative decision to initiate transfer, the stroke team (ie, stroke neurology and neurosurgery services, anesthesia team, nurse, and radiation technologist) is notified via page. The neuroscience intensive care unit charge nurse is also notified to facilitate timely postintervention admission. A series of subsequent pages are sent to the stroke team as additional information becomes available: confirmation of patient name and date of birth, departure time from the outside facility, and estimated time of arrival at our facility.

The patient arrives at the emergency room, bypassing the emergency department triage bay, where the patient is met by the neuroendovascular and stroke neurology teams and is taken directly to the imaging suite. A rapid neurologic
assessments, including determination of the NIHSS score, is performed on route to the computed tomography (CT) scanner, where noncontrast head CT and CT angiography with/without CT perfusion are obtained. Whether to proceed to the neuroendovascular suite is determined on the basis of clinical and radiographic assessment. If the patient is deemed a candidate for intervention, the patient is escorted directly to the neuroendovascular suite, where the anesthesia team and nursing staff are waiting. Thrombectomy procedures are routinely performed under conscious sedation, unless there is concern for airway protection. In cases with a compromised airway or a mental status that precludes safe administration of conscious sedation, the anesthesia team administers general anesthesia.

### Patient Population

During our pilot study (July 2015 through July 2016), 62 patients were triaged and managed using the Join application. Use of the Join application during this time period was at the discretion of the physician. Patients captured in this study include patients that were transferred from other hospitals, as well as those presenting to our emergency room. Since the pilot study, we routinely triage and manage all acute stroke patients using the Join application. Institutional review board approval was not required for this study.

**Join Mobile Smartphone Application**

A customized mobile smartphone application called Join was developed in an effort to streamline our Stroke 60 workflow model described above. Important features of this application include the following:

- Immediate notification to the entire treatment team of basic patient information and demographics (Figure 2)
- Automated time-stamping of events
- Real-time, secure communication among treatment team members
- HIPAA (Health Insurance Portability and Accountability Act)–compliant transmission of patient demographics and clinical information
- Real-time monitoring and communication of the patient’s exact position during transport using global positioning system (GPS)
- Generation of a summary document in portable document format (PDF) that can be uploaded into the electronic medical record

Time-stamped events include time of onset (or last known well time), time of IV-tPA (intravenous tissue plasminogen activator) administration, time when consent was obtained,

### Stroke 60 Pathway

The following table and diagram illustrate the acute stroke pathway.

#### Figure 1. Stroke 60 workflow algorithm. The Join application has been integrated into our Stroke 60 workflow.
time of arrival (door time), time of completion of imaging, arrival to the angiography suite, procedure start time (groin puncture), first pass time, and recanalization time. These events and their time stamps are recorded by a member of the treatment team (usually a nurse practitioner) and are immediately visible to the treatment team via the smartphone application (Figure 3).

Given the multiple stages of patient transport and the unavoidable obstacles due to our location in a major metropolitan area (eg, rush hour traffic, detours), a real-time GPS-based patient tracking system was developed and incorporated to inform treatment team members of the transport progress (Figure 4). From the moment that the transporting team logs into their mobile version of the Join application, all the stroke team members can follow the ambulance en route to the hospital—reminiscent of an Uber ride request.

After completion of the endovascular intervention and admission to the intensive care unit, the information is transmitted in the form of a summary document. It can be available as a PDF for printing and/or uploaded into the electronic medical record as a stroke code report.

Assessment of Join Application

Following our pilot trial of 62 patients, we administered a survey (questions listed in Table) to the treatment team members to determine the usability of the application. The survey was administered to the emergency medical service (EMS) personnel, radiology technologists, nurses, research personnel, advanced practice providers, and physicians.
Results

During this pilot trial, we triaged and managed 62 patients using the Join application. We found that the secure text communication feature facilitated the rapid delegation of tasks and ensured confirmation of their completion among the entire team. Additionally, this feature allowed for communication of deviations from the protocols (so-called “audibles”) when they were necessary due to various circumstances.

Automated time-stamping of events was performed for all patients. Summary reports also were obtained for all patients and successfully uploaded to the electronic medical record.

Following the pilot trial of the Join application, we administered surveys to the treatment team members to assess the application’s usability. The survey found a generally positive impression of the Join application (Figure 5 and Table). Of note, 87.5% of respondents found the application easy to use, and 82.5% of respondents recommended continuing to use the application as a method of team communication.

Discussion

To our knowledge, this is the first report describing the integration of a mobile smartphone application with GPS (patient tracking) functionality in the workflow and management of acute ischemic stroke patients. The Join application described here coordinates the activities and travel logistics of all facets of this workflow, including the patient, initial presenting hospital, transportation service (ambulance or helicopter), receiving hospital, associated physicians, and on-call treatment team members. This secure application is HIPAA-compliant and able to capture data that subsequently can be integrated as a permanent part of the patient’s electronic medical record.

Smartphones increasingly are becoming a part of our personal and professional lives, with more than two-thirds of physicians reporting their regular use. The use of smartphones and their mobile applications has similarly been increasing in the realm of acute ischemic stroke. To date, mobile applications have primarily been used in the setting of risk factor monitoring.

Figure 4. Real-time patient tracking feature of the Join application. A, The patient’s pickup time and location can be seen. B, Transport to the hospital can be tracked in real time.
and management,\(^3\) assessment of stroke severity (via NIHSS),\(^6\) and rehabilitation following stroke.\(^5\) While GPS technology has been used in stroke-focused mobile applications previously, it has only been used in a static way, locating the nearest treatment center.\(^1\) Here, we present the first report of a mobile smartphone application designed to track patient location, thereby helping to coordinate immediate endovascular treatment and management of acute ischemic stroke.

One potential limitation of this application is that it requires a team member to record data points in real time in the application. Although this is an added responsibility for one of the team members, our team did not perceive that this responsibility created any obstacle to patient care. Rather, the Join application interface allows for recording of these time points with a simple click on the smartphone screen, an action that typically takes a fraction of a second.

As seen from the results of the administered survey, the response to implementation of the Join application was generally positive. Of the groups surveyed, EMS personnel rated the application less favorably compared to hospital-based team members. Of EMS personnel surveyed, 52.4% reported that the application added extra work to the existing process. We hypothesize that this response may have been the foundation for an overall less positive response from this group. Despite this finding, 95.2% of EMS personnel felt the application was easy to use, and 85.7% recommended continued use of the application, which was actually slightly higher than the response from the group as a whole. One potential reason that they largely favored continued use of the application may be the ability to relay results from the hospital course, such as imaging and treatment, through the application. For example, we routinely transmit a picture of the retrieved thrombus through the application, which allows all members to see the results of their efforts. This is of particular benefit to the EMS personnel, who can often be left in the dark regarding a patient’s outcome following transport. Instead, through communication with Join, the findings and results of the patient’s treatment can be relayed to the entire team.

### Table. Survey Administered to Users of the Join Application

<table>
<thead>
<tr>
<th>Question</th>
<th>Strongly disagree</th>
<th>Disagree</th>
<th>Neutral</th>
<th>Agree</th>
<th>Strongly agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. I like the concept of the Join application</td>
<td>1</td>
<td>4</td>
<td>12</td>
<td>13</td>
<td>13</td>
</tr>
<tr>
<td>2. I have obtained information about transfers via Join earlier than the traditional method of pages/calls</td>
<td>1</td>
<td>4</td>
<td>7</td>
<td>11</td>
<td>17</td>
</tr>
<tr>
<td>3. I find that I have less downtime waiting for the patient due to the ability to track patient location</td>
<td>1</td>
<td>3</td>
<td>16</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td>4. Information has been reliable</td>
<td>1</td>
<td>6</td>
<td>16</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>5. I feel the data collected in Join should be made a permanent part of the patient medical record</td>
<td>1</td>
<td>4</td>
<td>13</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>6. It is an easy-to-use application</td>
<td>1</td>
<td>4</td>
<td>13</td>
<td>28</td>
<td>7</td>
</tr>
<tr>
<td>7. It adds extra work to an existing process</td>
<td>1</td>
<td>6</td>
<td>12</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>8. Information technology support is always accessible for problems that arise</td>
<td>1</td>
<td>4</td>
<td>24</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>9. I recommend continuing this method of team communication</td>
<td>1</td>
<td>6</td>
<td>14</td>
<td>19</td>
<td>19</td>
</tr>
</tbody>
</table>

![Figure 5. Results of survey administered to physicians, nurse practitioners, nurses, radiation technologists, and emergency medical service personnel using the Join application. For a list of survey questions, see Table.](image-url)
An additional benefit of the Join application is its inherent reduction in hand-offs. Since communication is transmitted to a text message thread that is available to the entire treatment team, there is decreased need for hand-offs between individual members of the team. Hand-offs are often necessary in patient care settings, but it is well recognized that higher numbers of hand-offs are associated with an increased incidence of medical errors. The ability to reduce or eliminate hand-offs will likely improve the efficiency and safety of care.

As those treating acute ischemic stroke know well, an effective and efficient treatment team is critical to the delivery of care. One often overlooked aspect of this is physician and team burnout. While the concept of physician burnout has become more recognized, burnout associated specifically with those treating acute ischemic stroke is less well studied. In a Japanese survey of 2564 physicians working in acute stroke care, the number of hours worked per week and the time spent in stroke care were positively associated with the severity of burnout. Interestingly, the study also found that burnout was less likely in accredited hyperacute stroke centers. The authors attribute this finding to the fact that these institutions had sufficient staffing, as required by the Japanese government per Joint Commission standards.

We believe the Join application will help alleviate treatment team burnout largely by maximizing time efficiency. Through instantaneous notification of patient location, the treatment team can time necessary preparations for the patient’s arrival, including their own arrival at the hospital, rather than waiting idle for an indefinite amount of time. Task assignment through secure messaging allows team members to “divide and conquer,” improving efficiency of workflow and reducing duplication of tasks such as calling the family for consent or screening for clinical trial inclusion. Secure messaging with EMS personnel permits communication with the transporting team and allows the team to be prepared for any changes in patient condition that may occur during transport. Additionally, for those patients who do not end up needing endovascular therapy, communication through Join instantly alerts all members of the team that the procedure has been cancelled, minimizing the amount of time spent in the hospital.

Lastly, while the application helps with efficiency, the ability to remotely follow a case to its conclusion may also aid with reducing burnout. In essence, it permits the entire team to see the fruits of their labor, regardless of whether or not they remain involved with the patient’s care. In a busy comprehensive stroke center such as ours, team members may be called in after hours as many as 2 to 3 times per week. Therefore, attention to team morale and burnout is critical for the retention of staff and continued improvement in the delivery of care.

The Join application described here represents the first generation of a real-time, mobile patient-tracking smartphone application. As such, it certainly has room for improvement. Our survey revealed an overall less positive response to the application by EMS personnel. Automation of EMS involvement in the application, rather than the current requirement of active sign-on, may be one improvement that may improve EMS personnel perception and streamline use of the application. Additional improvements may include addition of the EMS neurologic evaluation and transport care updates into the Join application time stamps.

Conclusion

In our initial experience, the Join application provided reliable, graphical, real-time tracking of patient location during transport, secure communication between treatment team members, and accurate time-stamping of critical events during the triage and management of patients with acute ischemic stroke. Our pilot experience has been positive, though qualitative in nature. Additional prospective and quantitative validation and continued work to improve the efficiency of stroke care are warranted.
References


DEVELOPING A SUCCESSFUL GLOBAL NEUROLOGY PROGRAM

Omar K. Siddiqi, MD, MPH; Merritt Brown, MD; Christine Cooper, MD; Masharip Atadzhanov, MD, PhD; Shabir Lakhi, MBChB, MMed, MPH; Igor J. Koralnik, MD

Author Affiliations: Global Neurology Program, Division of Neuro-Immunology, Center for Virology and Vaccine Research, Department of Neurology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts (Drs Siddiqi and Koralnik); Department of Internal Medicine, University of Zambia School of Medicine, Lusaka, Zambia (Drs Siddiqi, Atadzhanov, and Lakhi); Division of Neurocritical Care, Department of Neurology, University of Pennsylvania Health System, Philadelphia, Pennsylvania (Dr Brown); Movement Disorders Division, Department of Neurology, Medical University of South Carolina, Columbia, South Carolina (Dr Cooper); and Department of Neurological Sciences, Rush University Medical Center, Chicago, Illinois (Dr Koralnik).

Corresponding Author: Omar K. Siddiqi, MD, MPH, Beth Israel Deaconess Medical Center, 330 Brookline Avenue, Boston, MA 02215 (osiddiqi@bidmc.harvard.edu).

Previous Publication: This article was previously published in Annals of Neurology in February 2017. View this article online at https://doi.org/10.1002/ana.24863. Minor modifications have been made for this publication.

Introduction

In the last decade, the field of global neurology has gained prominence. The American Academy of Neurology formed a global health section that currently has over 300 members.1,2 Numerous academic departments now have global neurology programs that provide support to institutions in low- or middle-income countries (LMICs). These relationships often take the form of patient care, teaching activities, research projects, and resident electives. The regulations surrounding clinical electives overseas are also clearer.3 Residency applicants often ask program directors about global neurology opportunities when interviewing, suggesting that residency programs that lack appropriate opportunities will become less competitive. A well-developed global neurology program provides a dynamic element for a department while enhancing neurological activities at both institutions involved in the collaboration.

Establish Collaborations With Institutions in Resource-Limited Settings

The most important aspect of developing a global neurology program is to establish collaboration with an appropriate and willing partner. This is most commonly done with institutions in a resource-limited setting because they have the greatest needs. The initial steps in building this relationship can occur in several ways. Many academic institutions already have a presence at an overseas institution through other departments that can easily extend to neurology. In addition, residents often have preexisting connections from previous work experience or research activities in medical school that can help jump-start a program. Developing a relationship with a single institution more easily allows for the building of trust and for the host institution to see the benefit of the collaboration. It also provides the benefit of understanding the politics and practice of neurology in a different setting in order to enact meaningful change.

Zambian adult neurology trainees Lorraine Chishimba (left) and Mashina Chomba (right) with author Igor Koralnik, MD, at University Teaching Hospital, Lusaka, October 2018.
Involving a Senior Faculty Member

The establishment of a global neurology program benefits greatly from the involvement of a senior faculty member who has experience in starting a division or new program within a neurology department. Such a person does not necessarily need to have global health experience. The senior faculty mentor should be someone who is respected in the academic setting, understands how to get buy-in from the leadership, and can advocate how a global neurology program adds value to the department. Involvement of a senior faculty member can help legitimize the program. Individuals with a research background are ideal given that they can help junior investigators navigate the funding environment, help formulate viable research projects, and critique grant applications. Ideally, this individual has an interest in a subspecialty that is resonant with the health needs of the foreign partner as well as a research program and grant-writing ability to help generate funds in that setting.

Aim for Financial Sustainability

The early stages of developing a global neurology program may be quite challenging. Single-year fellowships or grant funding from organizations such as the Fogarty International Center, the American Academy of Neurology, and the World Federation of Neurology can help spearhead the effort. Department chairs can also provide seed money, but ultimately the program has to become financially viable. This is difficult given that there is no direct clinical revenue.

Philanthropy can play a role and should be cultivated in the parent and collaborating countries. Philanthropic donations cannot sustain a program alone, outside of sizable gifts that establish an endowment. However, they allow for unrestricted and bridging funds to help maintain a program. Anchoring a program in research is therefore the clearest way to access a steady funding stream. There are ample National Institutes of Health (NIH) and foundation grants available to fund neurological research in LMICs. This path is similar to research in other subspecialties of neurology. Academic productivity is measured in terms of publications and research accomplishments that can subsequently lead to larger funding opportunities.

Ideally, a program should have a combination of research and philanthropic funds to remain sustainable. Depending on the program, a faculty member may live in the partnering country full time, spend weeks to months at the overseas site, or provide services in the form of telemedicine or research support from the home institution. The ability to work in shifts, generate salary, and not be tied to an outpatient clinic lends itself to working overseas for extended periods. A subspecialty that can be practiced in isolated blocks of time and does not require long-term follow-up of patients, such as neurohospitalist, inpatient stroke specialist, or clinical neurophysiologist, is well suited to global health.

Encourage Multi-institutional Involvement in the Parent Country

Global neurology programs are stronger when they are multi-institutional in the parent country. It is important to have an “all hands on deck” approach rather than being proprietary, given the degree of need in most LMICs. Different institutions have varying degrees of expertise and resources to contribute. In addition, when multiple universities are invested in a common cause, such as improving neurological care in a resource-limited environment, it has the added benefit of generating research collaborations between institutions domestically and internationally that might not occur otherwise.

Indeed, the Fogarty International Center Global Health Scholars and Fellows Program, one of the largest grants through the NIH aimed at training global health researchers, requires that US universities form consortia to carry out their proposed activities.

Build Local Capacity

It is important that the collaborating institution in the LMIC derive a clear benefit from the partnership. The investment by the collaborating institution is magnified if the global neurology program improves local conditions of clinical care and
There Is No Single Correct Model

A number of academic neurology departments have developed their own unique global neurology programs. These vary in scope from well-established research programs to monthlong clinical rotations for residents or support for nascent neurology training programs. The activities are based on a combination of the needs of the country and the skill set and interests of the individuals involved. Successful programs demonstrate a long-term commitment to the partnering LMICs.

The Authors’ Experience

The development of the Global Neurology Program at Beth Israel Deaconess Medical Center (BIDMC) is one example of a program that evolved from a mere concept into a sustainable entity. The program initially started with a self-funded elective at the University Teaching Hospital (UTH) in Lusaka, Zambia, by Omar Siddiqi, MD, MPH, during neurology residency in 2005. This was facilitated by Gretchen Birbeck, MD, MPH, who has a long-standing research program in the country. There were several elements that helped it develop into a productive relationship between BIDMC and the University of Zambia School of Medicine. The only neurologist in Zambia at the time, Masharip Atadzhanov, MD, PhD, was academically active, had a track record of successful collaborations, and was interested in building up neurological services. At that point, Igor Koralnik, MD, who was at the time director of the neurology/HIV center at BIDMC and had a long-standing interest in human immunodeficiency virus and related infectious diseases, expressed an interest in helping to develop the collaboration. This collaboration resulted in a publication on the spectrum of neurological diseases in Zambia based on the resident elective. More important, this initial project provided preliminary data for future research proposals.

Our group then obtained research funding over several years through the Harvard University Center for AIDS Research, the Fogarty International Center, the American Academy of Neurology, and the National Institute of Neurological Disorders and Stroke. The primary benefit of this funding was to allow Dr Siddiqi, by that time a faculty member, to be based 10 months per year at UTH in Lusaka, Zambia, in order to carry out research studies. These grants resulted in publications that gave our program credibility. The head of the

A Rush Resident’s Zambian Experience

By Teresa M. Lee, MD

I had the honor of being the first resident from Rush University Medical Center (RUMC) to spend a month in Lusaka, Zambia, rotating at the University Teaching Hospital (UTH). A little background information: Zambia is a landlocked country in southern Africa and is about the size of Texas. Lusaka, the capital city, has a population of about 1.7 million people.

My day would begin by attending morning report with the medicine residents and another neurology resident rotating from Beth Israel Deaconess Medical Center (BIDMC). Sometimes we received consults then; otherwise, we went to the wards afterwards to sift through the paper charts for consults to see. We broke for lunch in the cafeteria—a hearty meal of nshima (maize) and ifisashi (ground pumpkin leaves and nuts)—then returned to seeing consults in the afternoon. We staffed consults with Dr Omar Siddiqi, an attending at BIDMC and assistant professor in neurology at Harvard Medical School, who lives in Zambia most of the year. On Wednesdays, we saw patients with him at the neurology clinic. By the time we arrived at 7 am, the patients would be lined up out the door, waiting to be seen.

Seeing patients in Lusaka was in many ways different than seeing patients in Chicago, but most striking of all was the difference in pathology. The prevalence of HIV in Lusaka is about 16%; this completely changed the way we formulated differential diagnoses. A stroke may be due to uncontrolled hypertension, but we also considered tuberculosis, Cryptococcus, and other diagnoses we rarely come across in the US. It was an incredible opportunity to expand the way I thought about “bread and butter” neurology and how different this can be based on the patient population.

It was also challenging and rewarding to adapt to working in a resource poor setting. Though UTH is a tertiary care facility, I was surprised or saddened on a daily basis about which diagnostic tests or therapeutic options were available. They had the ability to perform routine EEGs, EMGs, and MRIs, but they could not obtain a stat CT Head for a neurologic exam change or give tPA for a stroke.

Continued on page 24
Department of Internal Medicine at the University of Zambia School of Medicine, Shabir Lakhi, MBChB, MMed, MPH, continued to be supportive of strengthening the relationship between our institutions. Recognizing the value of the program, our neurology department has dedicated funds since 2013 to send 2 residents per year for a 1-month elective at UTH during their training. In addition, our Global Neurology Program has developed collaborations with academic institutions and nongovernmental organizations that include the University of Rochester School of Medicine and Dentistry, Michigan State University, the University of Liverpool, the Zambia AIDS Related Tuberculosis Project, and the Center for Infectious Disease Research in Zambia. As a result, we have hosted medical students, fellows, and senior faculty from all over the world. Our capacity-building efforts include helping to develop a molecular diagnostic laboratory for cerebrospinal fluid analysis, establishing a neurophysiology laboratory with 2 trained electroencephalography technicians, and mentoring Zambian medical and graduate students on neuroscience research projects.

**Future Plans**

After 10 years of a highly gratifying and mutually beneficial relationship, we are now in a position to achieve the most effective capacity-building effort needed to improve neurological care in Zambia: an in-country neurology training program. We have drafted a curriculum for a neurology training program adapted to the academic requirements of the University of Zambia School of Medicine. We hope to enroll the first group of trainees within 1 to 2 academic years. This program will result in the first generation of Zambian neurologists who can continue to build a neurological community without relying on resource-rich settings for support. That outcome will fulfill the goal inherent in any successful global neurology program: ensuring that local expertise endures independently. In turn, there will eventually be a cadre of local physician scientists who can engage in more extensive research collaborations with institutions throughout the world.

**Residents’ Perspectives**

During our elective at UTH in Lusaka, we both found neurology to be particularly well suited for a resource-limited setting due to its focus on localization through detailed history and physical examination. We were exposed to a wide spectrum of neurological diseases, such as tetanus, cerebral malaria, and African trypanosomiasis, that we otherwise would not encounter during our US-based training. In addition to the bolstering of diagnostic acumen and clinical exposure, a global neurology elective reveals a number of potential opportunities for advocacy, public health education, and, most important, capacity building in the host institution. In Zambia, we saw an unusually large number of strokes in

Rush resident Teresa M. Lee, MD, shown here consulting on a case with Dr Koralnik, describes her time working at University Teaching Hospital in Zambia as both challenging and rewarding and says it expanded her view of “bread-and-butter neurology” and how different this can be based on the patient population.
patients with untreated hypertension. This was attributed to many in the population having high-sodium diets and the lack of preventative health care. Whereas the United States has a strong focus on preventative care, in many resource-limited areas this has been a relatively new focus over the past few years. Neurology trainees from the United States can engage in meaningful medical educational activities in resource-limited countries, particularly when there is an ongoing, well-organized collaboration between institutions.

In summary, pursuing a global neurology rotation during neurology residency has many advantages and can help contribute to a well-rounded neurology education that is beneficial to both settings. From a resident perspective, the opportunity to practice neurology in a new culture, and in a resource-limited setting, requires skills in line with all the Accreditation Council for Graduate Medical Education core competencies: patient care, medical knowledge, practice-based learning, communication, professionalism, and systems-based practice. Altogether, our experience in Zambia proved to be the highlight of our residency.

Author Contributions: All authors contributed to the conception, design, and drafting of the manuscript.

Potential Conflicts of Interest: I.J.K. has participated in scientific advisory boards for Medimmune and Johnson & Johnson and receives royalties for chapters on neurology/HIV and progressive multifocal leukoencephalopathy in UpToDate.

Continued from page 22

They had IVIg, but the hospital might run out of stock (if the patient was wealthy, family members could purchase it from a pharmacist in the city). It was also a lesson on how to make do with less. No IV pole? The patients held their fluids up themselves. No LP kit? We made do with an IV cannula, some “spirits” (alcohol), and phlebotomy tubes. No electronic medical record? We wrote paper charts and paper orders. This experience helped me see what luxuries some small things can be, but also how much work goes into the process of creating and maintaining a hospital system and how adaptable people can be.

I can barely begin to describe how heartbreaking it was to see the volume of unmet needs. The wards were crammed with beds lined up next to one another, sometimes with a curtain or two to provide privacy. There were only a few nurses (or “sisters”) for all the patients, so family members would instead sit by the bedside to attend to the patients’ needs—feeding, turning, and changing them. Families could be seen outside the hospital washing clothing and drying them on the bushes. There were only 10 ICU beds and a much higher number of patients who would qualify for ICU care in the US. When a patient died, the family members would mourn publicly, wailing on the wards and in the hallways. It was frustrating and saddening to see that some deaths might be preventable. However, it was also an opportunity to see how we could make any small impact by helping treat patients, or by teaching medical students and residents about neurology. I gave lectures on the neurologic exam to residents and helped them practice their exam skills in clinic. I also moderated bedside presentations and teaching sessions for some 7th (final)-year medical students, and they were eager to learn. Despite the challenges of living and working there, it was rewarding and a joy to get to know some of the Zambians, both within and outside of the hospital.

Overall, I had an unforgettable time and am extremely grateful for the opportunity to have rotated at UTH. I am so excited for other Rush residents to go to Zambia and share in this experience.
References


Introduction

Cortical stimulation for functional brain mapping has become an important tool for neurosurgeons and neurologists in the treatment of perirolandic and dominant neocortical temporal lobe epilepsy. For those patients with medically intractable epilepsy, excision of the entire epileptogenic focus is essential for long-term, seizure-free outcomes. The epileptogenic focus is defined as the discrete anatomic location that generates a seizure, which can then spread to distant sites. The epileptogenic focus is defined as the discrete anatomic location that generates a seizure, which can then spread to distant sites. This presents a challenge for attempted resection due to anatomical proximity of the epileptogenic focus to functional brain, namely the motor and sensory cortex, and language areas. The purpose of cortical stimulation mapping is to identify these areas in order to create boundaries for surgical resection, and the technique is considered the gold standard for brain mapping.

Since cortical mapping was first implemented, a variety of approaches and parameters have been used without a determined set of standardized guidelines. Additionally, it is well established that there is significant variation in how patients respond to electrical stimulation. One patient may demonstrate motor, sensory, and/or language responses and/or electrographic afterdischarges at relatively low levels of stimulation, while another patient may require a larger stimulus to produce the same reaction. It has been hypothesized that individual factors, such as age, duration of disease, type of lesion, and other variables, may explain this discrepancy. Several studies have been conducted to investigate the influence of these factors, but none have definitively resolved these questions.

In our study, we retrospectively analyzed cortical stimulation mapping data from 92 patients with medically intractable epilepsy. These patients had presurgical evaluation, subdural electrode placement, and subsequent monitoring with intracranial electroencephalography (EEG) and cortical mapping in the intensive care unit. The purpose of our study is to identify specific patient characteristics and their effect on cortical stimulation, and discover the extent of variation in behavioral responses that exists among patients with epilepsy. It is our goal to identify standards for cortical stimulation that will allow for safer, more effective, and tailored mapping for each individual.

Materials and Methods

Study Group

This is an institutional review board–approved retrospective analysis using a prospectively maintained institutional epilepsy surgery database. Our study population consisted of consecutive patients who underwent subdural electrode placement by a single surgeon and then underwent subsequent cortical electrical stimulation mapping. The cortical stimulation mapping was performed by one of three experienced neurologists at our institution. Additionally, all patients underwent prolonged invasive subdural cortical electrode video EEG monitoring. Functional and epileptogenic areas were assessed in all patients by cortical electrical stimulation and intracranial EEG recordings. Data were collected from the charts of these patients and detailed mapping reports, regardless of whether the patient had a following resective surgery. Data from depth electrodes were excluded in our analysis. There were 187 total patients who underwent subdural electrode placement during
this time period, and out of these, 92 had completed mapping reports with either intraoperative pictures or scout imaging scans, so that the location of each electrode could be confirmed and included in the analysis.

Presurgical Evaluation

Each patient was initially evaluated by completing a comprehensive history and physical exam, including age of disease onset, seizure semiology, past surgeries, use of antiepileptic medications, and other past treatments. Patients underwent video EEG monitoring as well as appropriate imaging. For most patients, imaging included a 1.5-T MRI and, if negative, a 3-T MRI for selected cases. Some cases required additional imaging such as PET (positron emission tomography), SPECT (single-photon emission computed tomography), and SISCOM (subtracted ictal SPECT coregistered to MRI). Patients also underwent an intracarotid amobarbital procedure (Wada test). This information was used to determine the dominant cortex and the best type of electrodes and location for implantation.

Implantation of Subdural Electrodes

All surgeries were performed at a single institution by a single surgeon (R.W.B.). Electrodes used were either strip electrodes or a grid configuration. These consisted of stainless steel disks, each separated by 1 cm. Clinical information such as seizure semiology, imaging, and EEG data, as well as gross anatomic assessment of cortex structure, was used to guide placement of electrodes. Postoperative imaging, either x-ray or CT superimposed onto the MRI, was performed to confirm placement of the electrode contacts.

Intracranial EEG Monitoring and Cortical Stimulation Mapping

Intracranial EEG monitoring was performed immediately afterward and continued an average of one week after electrode implantation. Focal electrical stimulation of the cortex was carried out to determine the location of sensory, motor, and language areas of the cortex. Stimulation was performed to paired electrode contacts on the subdural grids and strips. Stimulation utilized a Grass SI2 biphasic stimulator constant current unit with 2-s trains, with 0.3 impulses, at 50 Hz and 1.5 to 14.5 mA. The duration was fixed at 2 s for all functions tested, as it was adequate for all modalities. Amplitudes were measured from zero to maximum, and they were biphasic. Generally, stimulation intensity was increased by 1.0 mA until an electrical afterdischarge or behavioral response was observed. The electrical intensity reached for each electrode pair was recorded as well as the location of that pair. All behavioral responses were noted, including speech arrest, motor activity, sensory changes; other behaviors not including speech, sensation, or motor activity, having the experience of typical aura or seizure; and pain, which is thought to be attributed to dural stimulation. With this information, stimulation mapping reports were generated for each patient, where functional brain area borders were identified and superimposed onto MRI or CT images.

Surgical Resection

Eighty-three patients (90.2%) underwent seizure focus resection. This involved a second craniotomy with removal of the electrodes and resection of the epileptogenic focus, which was guided by the mapping report information. Intraoperative electrocorticography was often performed before and after resection to further confirm removal of tissue involved in the epileptogenic focus. Once the tissue was removed, a sample was sent to the pathology department for tissue analysis.

Follow-up

Seizure frequency and severity were recorded from the last office visit. These outcomes were assigned a score according to the Engel Seizure Outcome Grading Scale (Class I: free of disabling seizures; Class II: rare disabling seizures [“almost seizure free”] or seizure-free intervals of 3 to 6 months; Class III: worthwhile seizure reduction [more than 75%]; and Class IV: no worthwhile improvement with seizure reduction less than 75%) and were also recorded for analysis. All patients had greater than 1 year follow-up.

Analysis

All relevant demographic features pertaining to each case and cortical stimulation sessions were cataloged, including age at surgery, sex, duration of disease, laterality and lobe location of electrodes, pathology results, MRI findings, and Engel score. The measurement data for each patient were determined with minimums, maximums, and means, and these were analyzed as a group and presented as mean ± standard deviation. Data compilation was performed using Microsoft Excel 2010 (Microsoft, Redmond, Washington), and additionally SPSS Statistics (Version 22.0; IBM, Armonk, New York) was used for data analysis. Descriptive statistics were used to report the baseline characteristics and outcome profiles of all patients, and a correlation analysis was performed to investigate the correlation between the variables explored and thresholds for stimulation, with a P value < .05 as significant. We then used a paired-sample t test to compare the means between our variables.

Results

Characteristics of Patients and Disease Pathology

A total of 92 patient cortical stimulation mapping reports were analyzed. There were 49 males (53.3%) and 43 females (46.7%) with an age range of 5 to 63 years. Electrodes were placed on the left hemisphere in the majority of patients (60.9%), and a small subset of patients had electrodes placed on both sides.
The duration of disease varied across patients. Pathology of the resection sample was recorded and categorized into the following groups: sclerosis/astrocytosis, cortical dysplasia, glioma, other, or none. There were 57 patients (62%) whose pathology was consistent with sclerosis/astrocytosis. The next most common group was pathology consistent with glioma, which included 12 patients (13%). Cortical dysplasia accounted for 6.5% of patients, and other findings such as cysts or hemorrhage accounted for 8.7% of patients. There were nine patients (9.8%) that did not have any findings on tissue analysis. Table 1 presents the characteristics and demographic data from the patient population.

Comparison of the Average Minimum, Maximum, and Mean Thresholds Across Different Behavioral Responses

The difference of stimulation threshold between the different behavioral responses was not as distinct as expected. It is important to note, when comparing the different behavioral responses, that the number of patients will not be the same since not all patients experienced a motor, sensory, or speech response; afterdischarge; seizure; or other response. Each patient had his or her own set of data regarding behavioral responses and the minimum, maximum, and mean thresholds to obtain these responses. For each patient, we recorded the response (if any) from cortical stimulation in different modalities, such as language, motor, sensory, afterdischarge, or seizure. After a mapping session, each patient had minimum, mean, and maximum values of current for each modality that was tested. These current values were then averaged from all patients to produce minimum, mean, and maximum values for each modality. For example, a patient in the group may have had 20 contacts that were stimulated, and out of those, several produced a motor response, several produced a sensory response, several produced an afterdischarge, and several produced no response even after stimulation to the highest threshold of 14 mA. The thresholds for all the motor responses were compared, and the mean, minimum, and maximum were calculated. The same was done for sensory, afterdischarge, and no-response contacts. These values were then compared with all patients in the whole group, and a total average of the mean, minimum, and maximum was calculated for each modality. The figures in Table 2 represent these data (the averages of all the individual data sets) to better understand the trends as a group. The average of the minimum thresholds for motor response was 4.15 mA ± 2.67, the average of the maximum thresholds was 7.41 mA ± 3.76, and the average of the mean of the thresholds was 5.50 mA ± 2.44. The average of the minimum thresholds for afterdischarge was 4.33 mA ± 2.37, the average of the maximum thresholds was 10.78 mA ± 2.83, and the average of the mean of the thresholds was 6.97 mA ± 2.24. The average of the minimum thresholds to induce typical seizure was 6.50 mA ± 3.76, the average of the maximum thresholds was 7.14 mA ± 3.54, and the average of the mean of the thresholds was 6.81 mA ± 3.57. Overall, there was no significant difference between the thresholds of sensory and motor

### Table 1. Demographic Data for All Mapping Reports Collected

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Number of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender</strong></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>43 (46.7)</td>
</tr>
<tr>
<td>Male</td>
<td>49 (53.3)</td>
</tr>
<tr>
<td><strong>Laterality of electrodes</strong></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>27 (29.3)</td>
</tr>
<tr>
<td>Left</td>
<td>56 (60.9)</td>
</tr>
<tr>
<td>Both sides</td>
<td>9 (9.8)</td>
</tr>
<tr>
<td><strong>Pathology</strong></td>
<td></td>
</tr>
<tr>
<td>Sclerosis/astrocytosis</td>
<td>57 (62.0)</td>
</tr>
<tr>
<td>Cortical dysplasia</td>
<td>6 (6.5)</td>
</tr>
<tr>
<td>Glioma</td>
<td>12 (13.0)</td>
</tr>
<tr>
<td>Other</td>
<td>8 (8.7)</td>
</tr>
<tr>
<td>None</td>
<td>9 (9.8)</td>
</tr>
<tr>
<td><strong>Age at surgery, y</strong></td>
<td></td>
</tr>
<tr>
<td>&lt;20</td>
<td>17 (18.5)</td>
</tr>
<tr>
<td>21-25</td>
<td>13 (14.1)</td>
</tr>
<tr>
<td>26-30</td>
<td>15 (16.3)</td>
</tr>
<tr>
<td>31-35</td>
<td>15 (16.3)</td>
</tr>
<tr>
<td>36-40</td>
<td>10 (10.9)</td>
</tr>
<tr>
<td>41-45</td>
<td>6 (6.5)</td>
</tr>
<tr>
<td>46-50</td>
<td>9 (9.8)</td>
</tr>
<tr>
<td>51-55</td>
<td>4 (4.3)</td>
</tr>
<tr>
<td>56-60</td>
<td>2 (2.2)</td>
</tr>
<tr>
<td>&gt;60</td>
<td>1 (1.1)</td>
</tr>
<tr>
<td><strong>Duration of disease, y</strong></td>
<td></td>
</tr>
<tr>
<td>&lt;5</td>
<td>12 (13.0)</td>
</tr>
<tr>
<td>6-10</td>
<td>19 (20.7)</td>
</tr>
<tr>
<td>11-15</td>
<td>11 (12.0)</td>
</tr>
<tr>
<td>16-20</td>
<td>13 (14.1)</td>
</tr>
<tr>
<td>21-25</td>
<td>9 (9.8)</td>
</tr>
<tr>
<td>26-30</td>
<td>11 (12.0)</td>
</tr>
<tr>
<td>31-35</td>
<td>6 (6.5)</td>
</tr>
<tr>
<td>36-40</td>
<td>4 (4.3)</td>
</tr>
<tr>
<td>41-45</td>
<td>3 (3.3)</td>
</tr>
<tr>
<td>&gt;45</td>
<td>4 (4.3)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>92 (100.0)</td>
</tr>
</tbody>
</table>
responses ($P = .630$), and also no significant difference between the thresholds of afterdischarge as compared to the motor or sensory response ($P = .208$ and $P = .109$).

Most striking is the degree of variability and wide range of thresholds seen between patients. Figure 1 provides a visual representation of the comparison of all 92 patient mean thresholds for the motor responses, sensory responses, and afterdischarge production.

**Comparison of Behavior Response Thresholds Between Different Lobes**

To directly compare the differences in thresholds between different anatomically regions, the locations of the electrodes were divided by lobes: frontal, frontoparietal, parietal, and temporal regions. For each location it was determined whether the electrode stimulation produced a behavioral response (including motor, sensory, or speech changes) or whether an afterdischarge or seizure was produced. The data are presented as the average of the minimum, maximum, and mean thresholds of all the patients. There was no significant difference between the thresholds of frontal lobe behavior and parietal behavior responses ($P = .181$). Also, there was no significant difference between the threshold of temporal behavior as compared to the frontal or parietal behavior response ($P = .340$ and $P = .344$); see Table 3.

**Factors Affecting Stimulation Thresholds**

A multivariate analysis was performed using all the patient characteristics recorded, namely age, sex, duration of disease, laterality of electrodes, pathology, and stimulation thresholds. There was no statistically significant difference found with these analyses (all $P$ values > .05).

---

**Table 2. Average of the Behavioral Response Threshold Means**

<table>
<thead>
<tr>
<th>Thresholds</th>
<th>Number of patients</th>
<th>Minimum (mA)</th>
<th>Maximum (mA)</th>
<th>Mean (mA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motor response mean</td>
<td>68</td>
<td>4.15 ± 2.67</td>
<td>7.41 ± 3.76</td>
<td>5.50 ± 2.58</td>
</tr>
<tr>
<td>Sensory response mean</td>
<td>63</td>
<td>3.50 ± 2.15</td>
<td>7.21 ± 3.59</td>
<td>5.26 ± 2.43</td>
</tr>
<tr>
<td>Speech response mean</td>
<td>41</td>
<td>4.47 ± 2.42</td>
<td>7.28 ± 3.41</td>
<td>5.75 ± 2.44</td>
</tr>
<tr>
<td>Afterdischarge mean</td>
<td>84</td>
<td>4.33 ± 2.37</td>
<td>10.78 ± 2.83</td>
<td>6.97 ± 2.24</td>
</tr>
<tr>
<td>No motor or sensory response mean</td>
<td>88</td>
<td>4.80 ± 3.31</td>
<td>12.78 ± 2.82</td>
<td>11.14 ± 3.01</td>
</tr>
<tr>
<td>Typical seizure mean</td>
<td>14</td>
<td>6.50 ± 3.76</td>
<td>7.14 ± 3.54</td>
<td>6.81 ± 3.57</td>
</tr>
<tr>
<td>Other responses mean</td>
<td>47</td>
<td>4.67 ± 2.61</td>
<td>8.01 ± 3.35</td>
<td>6.26 ± 2.60</td>
</tr>
</tbody>
</table>
Table 3. Stimulation Thresholds of Responses and Afterdischarge or Seizure Production, by Region

<table>
<thead>
<tr>
<th>Thresholds</th>
<th>Number of patients</th>
<th>Minimum (mA)</th>
<th>Maximum (mA)</th>
<th>Mean (mA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frontal lobe behavior mean</td>
<td>69</td>
<td>3.99 ± 2.64</td>
<td>8.37 ± 3.83</td>
<td>5.98 ± 2.68</td>
</tr>
<tr>
<td>Frontal lobe AD/seizure mean</td>
<td>65</td>
<td>4.99 ± 2.92</td>
<td>8.99 ± 3.55</td>
<td>7.17 ± 2.87</td>
</tr>
<tr>
<td>Frontoparietal lobe behavior mean</td>
<td>66</td>
<td>4.01 ± 2.11</td>
<td>6.21 ± 3.34</td>
<td>5.04 ± 2.43</td>
</tr>
<tr>
<td>Frontoparietal lobe AD/seizure mean</td>
<td>29</td>
<td>6.05 ± 3.96</td>
<td>7.53 ± 4.08</td>
<td>6.66 ± 3.75</td>
</tr>
<tr>
<td>Temporal lobe behavior mean</td>
<td>43</td>
<td>3.89 ± 2.80</td>
<td>7.48 ± 4.03</td>
<td>5.90 ± 3.03</td>
</tr>
<tr>
<td>Temporal lobe AD/seizure mean</td>
<td>56</td>
<td>3.86 ± 1.63</td>
<td>9.73 ± 3.30</td>
<td>6.39 ± 2.01</td>
</tr>
<tr>
<td>Parietal lobe behavior mean</td>
<td>63</td>
<td>4.58 ± 2.87</td>
<td>6.25 ± 3.33</td>
<td>5.40 ± 2.92</td>
</tr>
<tr>
<td>Parietal lobe AD/seizure mean</td>
<td>49</td>
<td>5.19 ± 3.01</td>
<td>7.15 ± 3.19</td>
<td>6.20 ± 2.91</td>
</tr>
</tbody>
</table>

Abbreviation: AD, afterdischarge.

Discussion

Cortical stimulation mapping is a critical tool in epilepsy surgery\(^6-12\) and brain tumor surgery\(^1\).\(^11\)-\(^15\) Exact parameters for obtaining a physiological response and for avoiding afterdischarges and clinical seizures have not been firmly established. Surgeons use cortical stimulation both extraoperatively and intraoperatively for localizing seizure focus and functional areas.\(^3\) However, intraoperative mapping faces unique challenges. It is limited by time and cooperativity of the patient. Strong narcotics may alter responses to stimuli, and observed behaviors of the patient can be unreliable due to lower levels of consciousness. It is for these reasons that extraoperative mapping is preferred by some centers and is performed during the interim between electrode placement and resection.\(^1\)\(^5\)\(^7\) However, regardless of when mapping is performed, the challenge remains to efficiently elicit motor, sensory, or language responses of functional brain while avoiding the production of afterdischarges. This is problematic because afterdischarges are correlated with induction of seizures and the need for increased antiepileptic drugs. Furthermore, the spread of afterdischarges to adjacent tissue may alter the excitability and produce unreliable clinical manifestations.\(^1\)\(^6\) Unlike what is seen so far in the literature, our results indicate that the threshold for afterdischarges is not significantly higher than those for sensory, motor, and speech responses. This is different than the findings published by Guojun and colleagues, who reviewed the cortical stimulation parameters for 21 patients with refractory rolandic epilepsy. They found that the mean thresholds for motor response, sensory response, and afterdischarge were 3.48 ± 0.87, 3.86 ± 1.31, and 4.84 ± 1.38 mA respectively.\(^7\) Our results indicate that at any electrical stimulation level, any behavioral or electrographic response may occur. This implies that clinicians need to achieve at least these intensities before the location can reliably be called nonfunctional.

Additionally, we found that there was high variability between different patients and even between different cortical regions within the same patient. The minimum threshold to create an afterdischarge or induce a seizure varies from patient to patient and at different times or locations within the same patient, and can fluctuate depending on time interval between seizure, density of interictal discharges, drug treatment, and status of drug withdrawal.\(^7\) Variability in threshold for afterdischarge production is well known, as afterdischarge production is thought to be not a graded response, but rather an “all or nothing” response that is produced once a critical number of neurons are depolarized.\(^16\)\(^18\) Therefore, lower neuronal density or other abnormalities may raise the threshold for afterdischarge and explain the wide ranges seen in these patients.

It has been assumed that patients with epilepsy may have different parameters for stimulation mapping than patients with brain tumor.\(^1\)\(^9\)-\(^12\)\(^19\)-\(^21\) The presumption is that the cortex may be hyperexcitable due to the seizure disorder and the brain alterations occurring over time that may even change a patient’s neuropsychiatric profile.\(^19\)\(^22\)-\(^24\) In our review of the cortical stimulation parameters in our large series of patients with epilepsy undergoing mapping, we did not find a clear indication that stimulation parameters are significantly different from previous reports of cortical mapping in brain tumor patients.

Our hypothesis was that certain patient characteristics affect threshold response levels and that correlations that serve as a predictive model for tailored brain mapping can be found. However, the data collected were unable to support this hypothesis. While there have been past studies that found correlations between age of the patient and duration of disease with the stimulation thresholds needed to create a response,\(^2\)\(^16\) our data did not find any relationship with these variables.

This study has overarching implications about the practice of electrical stimulation mapping. While previously it was understood that lower stimulation thresholds will yield motor and sensory responses and higher thresholds will produce afterdischarges and seizures, our analysis did not demonstrate such patterns. The subdural electrode arrays were placed over...
areas that were considered to possibly be involved in the patient’s epilepsy and over adjacent cortex thought to possibly have eloquent cortex. Afterdischarges were found in both regions, without a clear pattern for location of afterdischarges. To our knowledge, our data set represents the largest study population of patients specifically exploring stimulation parameters in patients who underwent extraoperative brain mapping. This not only will affect brain mapping for epilepsy surgery but also may hold significance in brain mapping for tumor surgery, which is traditionally mapped with the lowest possible stimulation thresholds. Such practice may be vulnerable to false negatives as cortical areas may require higher thresholds to elicit behavior.

One of the main strengths of our study is the consistency of the stimulation mapping process. This was carried out by one of only three neurologists and carefully documented in a mapping report in the same manner. Since all cortical stimulation was performed extraoperatively, sufficient time was given with the patient to ensure proper interpretation of behavioral responses. Limitations of this study pertain to the retrospective nature of the study design; some reports were excluded due to incomplete data, especially those from before electronic medical records were implemented at our institution and the development of graphic programs to present reconstructed images with the cortical grids. Mapping reports were only included if they had completed data, including images to localize the electrodes to a cortical lobe. For future investigation, it would be useful to compare the location of afterdischarges and the location of the epileptogenic zone and evaluate if there is a significance in proximity. However, these data were not available in our set. In addition, our data set does not have information regarding antiepileptic drug withdrawal, antiepileptic drug loading dose, and the distance of the cortical mapping from the last seizure.

Conclusion

This study illustrates that electrical stimulation mapping has significant variability in the stimulation thresholds necessary to elicit behavioral responses. Sometimes, thresholds as high as 14.5 mA are required to produce these responses. Finally, there seem to be no predictive factors based on location of the contacts or patient characteristics that can alter stimulation thresholds.

**Conflict of Interest Statement:** The senior author, Richard W. Byrne, MD, is a consultant for Integra and Stryker. He also owns patents related to cortical mapping. There are no other conflicts of interest or financial relationships to disclose.
References


RUSH EPILEPSY CENTER:
A Well-Rooted Tradition of Excellence Branching Out to the Future

Rebecca O’Dwyer, MD; Marvin A. Rossi, MD, PhD; Andrea Bermeo-Ovalle, MD

Author Affiliations: Department of Neurological Sciences, Rush University Medical Center, Chicago, Illinois.
Corresponding Author: Rebecca O’Dwyer, MD; Department of Neurological Sciences, Rush University Medical Center, 1725 W. Harrison St, Suite 855, Chicago, IL 60612 (rebecca_odwyer@rush.edu).

Introduction
Living with the uncertainty of having a seizure at any given time is one of the greatest challenges patients and families affected by epilepsy face every day. Seizures are often debilitating and entail restrictions, social isolation, cognitive impairment, and medication side effects. Having a multidisciplinary team of dedicated professionals working not only to control seizures but also to ensure that life does not stop for seizures is paramount. The Rush Epilepsy Center brings together a comprehensive group of professionals from multiple health care specialties to enable patients to lead full lives.

The Rush epilepsy tradition started with the late Frank Morrell, MD. After training under Herbert Jasper, MD, PhD, at the Montreal Neurological Institute and chairing the Department of Neurology at Stanford University, Dr Morrell moved to Chicago in 1972 to establish the Rush Epilepsy Center and start the surgical epilepsy program. Dr Morrell and his wife, Leyla de Toledo-Morrell, PhD (Figure 1), combined innovative clinical work and research that would result in novel concepts in the understanding of the pathophysiology of epilepsy and learning, including brain plasticity and secondary epileptogenesis.1 He started employing cutting-edge therapies such as the implementation of new surgical techniques, making a tangible impact in the diagnosis and treatment of patients living with epilepsy and its complications.

Today, the Rush Epilepsy Center is the largest operation devoted to epilepsy care in the Chicago area, with a dedicated 10-bed inpatient epilepsy monitoring unit, a 5-bed pediatric monitoring unit, and 15 portable units for remote electroencephalographic (EEG) monitoring in the intensive care setting. The Rush Epilepsy Center has been consistently accredited as a level 4 epilepsy center by the National Association of Epilepsy Centers, the highest possible designation.

The Rush Epilepsy Center provides care for more than 5000 patients every year, addressing the multidimensional needs of each patient, including medical, surgical, emotional, cognitive, and social aspects. Every part of patients’ well-being is an integral part of the Rush mission. Following this tradition of excellence, innovation, and collaboration, the center provides in-depth expertise and support to children and adults with epilepsy through specialized clinics, state-of-the-art clinical and surgical facilities, and dedicated basic and clinical research laboratories (Figure 1) for active pursuit of innovative technologies and treatments.

Figure 1. Leyla de Toledo Morrell, PhD, and her husband Frank Morrell, MD, established a strong foundation for the Rush Epilepsy Center with innovative research and cutting-edge therapies.
Dietary Treatments for Patients With Epilepsy: Improving Outcomes, Risk Factors, and Quality of Life

Our dietary clinic for patients with epilepsy, unique in Chicago, is one of very few in the United States. A registered dietitian nutritionist (with specialty training in epilepsy diets) and an epileptologist work in conjunction with the patient’s primary neurologist. Modified ketogenic diets, similar to modified Atkins diets and low glycemic index treatment, are primarily used, as opposed to the more restrictive classic ketogenic diet. The diet is individualized to the needs of each patient, based on epilepsy syndrome, seizure type and frequency, medical history, family support, and nutritional needs. A regularly scheduled formal lecture is given to patients and caregivers along with an individualized diet plan and routine follow-up.

Established in 2013, the clinic has treated more than 300 patients. Ketogenic therapy has demonstrated efficacy in reducing seizure frequency by ≥50% in approximately 45% of adults following ketogenic diets and modified ketogenic diets. Additionally, researchers have reported improvement in seizure severity and quality of life with minimal side effects. The clinic welcomes all patients with epilepsy, regardless of seizure intractability, as the benefits of the dietary treatments are extensive. Dietary treatment should be part of the comprehensive management of every patient with epilepsy.

Epilepsy Care for Older Adults: Complex Situations Require a Team Approach

One in 4 newly diagnosed patients with epilepsy is 65 years or older, and the risks of seizures and epilepsy increase with age. Seizures are often difficult to identify because they are less likely to secondarily generalize in older adults but rather present as discrete episodes of confusion, lapses in memory, falls, dizziness, brief repetitive movements, or nonspecific sensory changes. People are more likely to blame the aging process than to think of a seizure, delaying accurate diagnosis up to 1.7 years. To ensure a correct diagnosis, thorough evaluation is important. The cause of epilepsy in approximately half of older adults remains unknown; recognized causes include stroke, traumatic head injury, neurodegenerative disorders, and neoplasms of the central nervous system. The multimorbidity of patients not only complicates diagnosis but also poses therapeutic challenges.
The Rush Epilepsy Center opened the first comprehensive epilepsy clinic for older adults in the Midwest (Figure 2). The clinic comprises a multidisciplinary team, including a dedicated social worker and a pharmacist, and has close ties with the geriatrics, stroke, memory, psychiatry, and movement disorder clinics. As part of Rush’s Center for Excellence in Aging, this clinic adopts many touchstones of geriatric care—such as including caregivers in the treatment plan—while applying specialty epilepsy care, and is working to set a new standard of care for this often undertreated population.

The Northern Illinois Rural Population Health Initiative

In collaboration with the Epilepsy Foundation of North Central Illinois, the Rush Epilepsy Center co-founded an innovative population health rural ambulatory care initiative. The CARF-accredited initiative utilizes novel ‘communication-connectivity strategies’ managed by a progressive community-based coordination hub. The McHenry County-based hub both delivers and coordinates specialized health care to children and adults with medically intractable epilepsy and co-morbid mental health disorders. Its services include an integrated brain injury program.

The initiative provides a transformational community-based population health delivery model for nearly 1,000 rural residents living in multiple Northern Illinois rural communities. It proactively follows specialized health care utilization patterns of individuals living within their own county. Weekly video visits connect rural patients with a geographically distant epileptologist and pharmacist (SinfoniaRx), with onsite case coordinators, nurse clinician/practitioner, and scribe. Scalable efficient mobile health and data management strategies are developed at the Chicago campus’ Rush Neuroengineering Laboratory (synapticom.net). Connectivity protocols interface a custom-built electronic health record with mobile and wearable technologies, implantable medical devices, augmented reality–based assessment tools, and coordination of all pertinent medical and community-based psychosocial resources.

The driving force of the rural community hub includes 6 full-time case coordinators, a community-based Rush pediatric mental health nurse practitioner, family nurse practitioner, Rush Epilepsy Center-based epileptologists, information technology software developers, and biomedical engineers. The site offers a fertile training environment for doctoral students enrolled in the Rush Integrated Biomedical Sciences graduate program, and advanced practice nursing students.

Validating the success of such a comprehensive community-based strategy is critical to understanding its future utility in providing cost-efficient, comprehensive epilepsy-related health care both regionally and at a national level.

Neuromodulation: Approaching Excitation-Related Problems With Electrical Stimulation Solutions

Three neuromodulatory treatment options have been approved by the US Food and Drug Administration (FDA) for patients with medically refractory epilepsy. The Rush Epilepsy Center has been involved in pivotal clinical trials for all 3 medical devices and has extensive experience with each.

Responsive neurostimulation is a small skull-based stimulation system implanted to monitor a patient continuously for seizure activity. On-demand tuned stimulation pulses are delivered at the onset of a seizure to terminate the early seizure phase and eventually decrease breakthrough seizures (Figure 3). Rush was one of the first centers to study this device in patients and has 14 years of experience with the use of this system.¹²

Vagus nerve stimulation (VNS) involves the use of an implantable chest-based stimulator that sends regular brief pulses through the vagus nerve in the neck to reshape

---

Figure 3. Rush Neurosurgeon Sepehr Sani, MD, placing RNS electrode (A) as guided by white matter tractography used to define the epileptogenic circuit (B).
medication-resistant epileptic brain circuits. The newest version of the device uses heart rate-sensing technology to detect seizure onset. Rush has more than 25 years of experience with the VNS device and follows over 400 patients. The center is currently enrolling patients in a new multicenter VNS clinical trial that will employ novel microburst pulse settings.

Deep brain stimulation was recently approved by the FDA for use in patients with medically refractory epilepsy. After participating in the SANTE (Stimulation of the Anterior Nucleus of the Thalamus) trial, Rush is able to use this experience and offer this new treatment option to our patients.

Multimodal Surgical Planning: A Comprehensive Approach in the Search for the Epileptogenic Zone

The success of epilepsy surgery depends on correctly identifying the entire epileptogenic region for complete resection of the underlying abnormality. At Rush, we utilize high-resolution, 3-dimensional MRI along with high-density EEG source modeling of ictal and interictal epileptiform activity to provide state-of-the-art localization of surgically amenable areas. Additionally, we improved on these methods by combining quantitative MRI techniques, such as the measurement of cortical thickness (Figure 4) and voxel-based morphometry (Figure 5), with 3-dimensional EEG source modeling to provide supplementary 3-dimensional multimodal visualization of brain abnormalities. This method allows the superimposition of abnormal function and structure for improved detection and planning of the removal of the patient’s brain abnormality. Our ictal SPECT (single-photon emission computed tomography) neuroimaging program was established in 2002. The service exists as the only formalized ictal SPECT monitoring service in the region and includes its own dedicated SPECT scanner. Our institution has 1 of only 5 recently FDA-approved high-resolution 72-detector scanner systems in the world. The Rush Epilepsy Center’s SPECT service facilitates mapping of the ictogenic cortex by imaging early ictal transient blood flow changes. Specialized computer software matches the seizure-onset SPECT scan with a second SPECT scan acquired between seizures. Baseline blood flow patterns are subtracted from the seizure-onset pattern and then coregistered to the patient’s MRI (called SISCOM, from subtracted ictal SPECT coregistered to MRI). This information pinpoints the seizure onset region to facilitate surgical resection of the abnormality. Additionally, we are using MRI to develop novel in vivo structural markers for epilepsy. These markers will help determine the epileptogenic focus and laterality of epileptogenic regions and how these regions relate to cognitive decline in patients with intractable epilepsy.

High-Density EEG: Better Sampling Results in Better Resolution

Noninvasive EEG is used to localize interictal and ictal epileptiform discharges as well as seizures. This information is used in the diagnosis of epilepsy and planning of epilepsy surgery. The traditional electrode arrangement employs a 21- to 32-electrode montage to aid in localizing the source of these abnormal discharges (Figure 6). At the high-density EEG laboratory at Rush, we can record, analyze, and localize the information from an arrangement of 128 to 256 simultaneous electrodes, and we can specifically digitize these electrodes to coregister this electrical brain activity to the individual brain MRI (Figure 7). This technology allows us to precisely localize the area of the brain responsible for these abnormal discharges and correlate that information to other imaging and functional modalities through a noninvasive, ambulatory procedure.
The Rush Epilepsy Center is dedicated to training future neurologists, neurophysiologists, and epileptologists. Each year, 1 epilepsy fellow and 4 clinical neurophysiology fellows are trained through programs approved by the Accreditation Council for Graduate Medical Education. Moreover, faculty are actively involved in the education of neurology resident trainees and neurology trainees who come to Rush from a variety of international countries to enhance their clinical epilepsy and neurophysiology knowledge.

During training, fellows have intimate exposure to and education in long-term video EEG monitoring in various settings, including the epilepsy monitoring unit and the adult, pediatric, and neonatal intensive care units. Additional opportunities are available for further development of skills focused on intracranial EEG monitoring, electrical stimulation, evoked potentials, manual hippocampal volume analysis, and electrocorticography. Our graduates ultimately spread throughout the United States and beyond, providing excellent care to patients and contributing to research in the field of epilepsy.

Exciting Times to Be in the Field of Epilepsy

When Dr Frank Morrell founded the Rush Epilepsy Center, he built it on innovative clinical work, thought-provoking research, and education—a tradition that thrives today. The Rush Epilepsy Center offers patients state-of-the-art epilepsy care and surgery, groundbreaking specialized clinics, and access to a host of clinical trials and treatment devices, while educating the next generation of neurophysiologists and epileptologists. As the field of epilepsy evolves, the Rush Epilepsy Center will remain on the forefront of efforts to eliminate seizures and maximize quality of life for all patients.
References


15. Stoub T, Sharma M. Decreased parahippocampal white matter volume in temporal lobe epilepsy. Poster presented at: American Epilepsy Society Annual Meeting; December 2-6, 2016; Houston, TX.

CERVICAL SPINE DEFORMITY—PART 1:
Biomechanics, Radiographic Parameters, and Classification

Lee A. Tan, MD; K. Daniel Riew, MD; Vincent C. Traynelis, MD

Introduction

The fundamental functions of the cervical spine include transmitting axial load from the cranium, maintaining horizontal gaze, allowing normal head and neck movement, and protecting important neurovascular structures such as the spinal cord, nerve roots, and vertebral arteries. A healthy and normally functioning cervical spine is the basis for performing many activities of daily living and is essential for maintaining a good quality of life. Cervical spine deformities, however, can significantly limit the normal function of the neck and thereby diminish the patient’s quality of life.

The most common form of cervical spine deformity is cervical kyphosis. These patients most commonly present with neck pain but may also have myelopathy and may have sensorimotor deficits due to compression of the neural elements and impaired cord perfusion from an overstretched spinal cord. If the kyphotic deformity is severe (chin-on-chest deformity, dropped head syndrome, etc), patients can have significant difficulty with swallowing and maintaining horizontal gaze. Surgical treatment is often required for these symptomatic patients. The general goals of cervical spine deformity surgery include correction of deformity, restoration of the horizontal gaze, decompression of the neural elements as necessary, solid arthrodesis to maintain the surgical correction and spinal alignment, and avoidance of complications.

Specific surgical techniques include anterior cervical disectomy and fusion, anterior cervical corpectomy, anterior osteotomy, Smith-Petersen osteotomy, pedicle subtraction osteotomy, or any combination of these techniques. Regardless of which specific surgical approach is used, a solid understanding of spine biomechanics, a thorough preoperative neurological examination, and a detailed review of preoperative images, along with careful surgical planning and meticulous surgical techniques, are essential to ensure the best clinical outcome in cervical deformity correction.

We aim to provide an overview of cervical spine deformity, including, in Part 1, biomechanics, radiographic parameters, and classification; in Part 2, treatment algorithms and anterior techniques; and, in Part 3, posterior techniques, clinical outcome, and complication avoidance.

Biomechanics of the Cervical Spine

The cervical spine is a weight-bearing mechanical structure with 6 degrees of freedom of movement. The principal motions of the cervical spine include flexion/extension, axial rotation, and lateral bending, along with a small amount of coupled anterior/posterior translational movements along the Cartesian coordinates (Figure 1). The cervical spine is able to move within the neutral zone with relatively little force and therefore requires very little energy expenditure from the paraspinal muscles. Additional movement beyond the neutral zone, however, requires more effort to overcome the elastic force from the soft tissues; therefore, this zone is called the elastic zone. Adding the movement realized in both the neural and elastic zones provides the total range of motion (ROM) at a given segment. An abnormal increase in neutral zone or ROM may indicate ligamentous injury or spinal instability.

The global physiological ROM in the cervical spine is approximately 90° of flexion, 70° of extension, 20° to 45° of lateral bending, and up to 90° of rotation on each side. The atlanto-occipital joint is a strong synovial joint formed by the...
The interface between the convex occipital condyle and the concave C1 superior articular facet. They form a ball-and-socket joint reinforced by a strong joint capsule. This configuration allows a large degree of flexion/extension, but very little movement in lateral bending or axial rotation. The atlantoaxial joint includes 4 synovial joint interfaces, which exist between the anterior arch of C1 and the odontoid process, the odontoid process, and the transverse ligament, as well as the paired C1-2 facet joints. In contrast to the atlanto-occipital joint, the atlantoaxial joint allows a large degree of axial rotation, with more limited flexion/extension and lateral bending. The articular cartilages on the atlantal and the axial facets are both convex, therefore forming a “biconvex” joint filled with fibro-adipose meniscoids. In the neutral position, the apexes of the 2 articular surfaces rest on each other. When rotation occurs, the C1 inferior facet glides posteriorly over the C2 superior facet on the ipsilateral side and glides anteriorly over the C2 superior facet on the contralateral side to facilitate a smooth rotational movement. Panjabi et al. found that the ROMs for flexion, extension, lateral bending, and axial rotation were 3.5°, 21.0°, 5.5°, and 7.2°, respectively, at the atlanto-occipital joint and 11.5°, 10.9°, 6.7°, and 38.9° at the atlantoaxial joint. The greatest motion between 2 vertebral segments is the axial rotation at the atlantoaxial joint, with the neutral zone (29.6°) accounting for 75% of this motion. The subaxial cervical spine (C3 through C7) is responsible for the remainder of ROM in the cervical spine.

Several basic physical parameters dictate the biomechanical properties of the cervical spine. These include mass (m), force (F), standard gravity (g), moment arm (L), bending moments (M), and instantaneous axis of rotation (IAR). In the upright position, the head exerts a gravitational force on the cervical spine with the magnitude \( F = m \times g \). This gravitational force then creates a forward bending moment \( M \) around a fulcrum of rotation, also known as the IAR. The magnitude of the bending moment is calculated by \( M = F \times L \), in which \( L \) is the distance between the IAR and the center of gravity line.

The center of mass (COM) of the cranium is estimated to be approximately 10 mm anterior to the supraturagic notch just above the head of the mandible. In a normally aligned lordotic cervical spine, the posterior tension band and paraspinal muscles counterbalance the forward bending movement created by the weight of the head, thus maintaining the natural cervical alignment (Figure 2). The axial load from the cranium is initially transferred from occipital condyles to the C1 lateral masses, then to the C1-2 facet joints and C2 lateral masses, and is subsequently distributed to the rest of the spinal column via the C2-3 intervertebral disk and facet joints. The facet joints in the subaxial cervical spine bear about two-thirds of the axial load, while the remaining one-third of the axial load is transmitted via the intervertebral disks.

When cervical kyphotic deformity is present, the head COM moves anteriorly and the movement arm \( L \) increases relative to the IAR, thus creating a larger bending moment \( M \). The resultant larger bending moment requires greater paraspinal muscle contraction to keep the head erect, which in turn can cause muscle fatigue and pain. In addition, kyphotic cervical deformity shifts the axial load anteriorly and thus can potentially accelerate cervical disk degeneration. Decreased disk height from degenerative changes can cause more cervical kyphosis, thus creating the notion “kyphosis begets kyphosis.”

Furthermore, kyphotic deformity can also lead to stretching and lengthening of the spinal cord, resulting in increased tension and impaired microcirculation, eventually leading to spinal cord ischemia and resultant myelopathy over time. However, one should keep in mind that not all kyphotic deformities are symptomatic. It has been estimated that cervical kyphosis can be found in 2% to 35% of asymptomatic patients. It has been estimated that cervical kyphosis can be found in 2% to 35% of asymptomatic patients.

Figure 1. An illustration demonstrating the 6 degrees of freedom in the cervical spine.

Figure 2. A lateral x-ray showing natural spinal alignment with proportional cervical lordosis, thoracic kyphosis, and lumbar lordosis, along with the center of gravity line passing through the femoral heads demonstrating good sagittal balance.
Radiographic Parameters

There are several radiographic parameters commonly used to assess the cervical spine, including cervical lordosis (CL), C2-C7 sagittal vertical axis (SVA), chin-brow vertical angle (CBVA), T1 slope (T1S), thoracic inlet angle (TIA), and neck tilt. An overview of these parameters is provided below along with a brief discussion of cervical deformity classification.

Cervical Lordosis

In 1977, Bagnall et al. found that at 9.5 weeks of gestation, 83% of fetuses had CL, 11% had a military configuration, and only 6% of fetuses had cervical kyphosis. From this result, the authors deduced that 94% of fetuses began to use their posterior cervical muscles to form cervical curve by 9.5 weeks of gestation. This finding supports the theory that CL begins to form even before birth, develops more as an infant learns to support the weight of the head by sitting up, and further increases after standing and walking begin. However, there is currently no universally accepted definition of “normal” CL. By convention, a lordotic alignment is usually reported as a negative angle, whereas a kyphotic alignment is generally reported as a positive angle. The 4 most common methods for measuring CL include the modified Cobb method (mCM), Jackson physiological stress lines (JPS), Harrison’s posterior tangent (HPT) method, and the Ishihara index (Figure 3).10-12

To measure CL using the mCM, 2 lines are drawn along the C2 and C7 inferior end plates first; then additional lines perpendicular to the first 2 lines are drawn, respectively, and the angle subtended by the perpendicular lines equals CL. Alternatively, most modern digital imaging software has the built-in capability of measuring lordosis by simply drawing lines tangent to the end plates of the vertebrae of interest and measuring the angle between them as described by Drexler.13 Some authors also use a line connecting the anterior and posterior tubercles of C1 instead of the end plate of C2 as the upper reference line to estimate CL. The JPS can be obtained by drawing a line along the posterior vertebral walls of C2 and C7, respectively; the intersection of these 2 lines will give an estimate of CL. The HPT method involves drawing lines parallel to the posterior surfaces of all cervical vertebral bodies from C2 to C7 and then summing all the segmental angles for an overall cervical curvature angle. The Ishihara index, also known as the cervical curvature index, can be calculated by the following steps: (1) draw a line from the posterior-inferior edge of C2 to the posterior-inferior edge of the C7 vertebra; (2) draw 4 lines starting from the posterior-inferior edges of the C3, C4, C5, and C6 vertebrae, perpendicular to the previous line connecting C2 to C7; (3) calculate the total length of the 4 horizontal lines at C3, C4, C5, and C6, and then divide it by the length of the line connecting C2 to C7. A higher ratio of the Ishihara index corresponds to a more lordotic cervical spine, whereas a lower ratio corresponds to a “straighter” cervical spine. If the cervical spine is perfectly straight, then the Ishihara index equals zero.

Hardacker et al.14 reported an average C1-C7 lordosis of -39.4° ± 9.5° after studying 100 asymptomatic volunteers. The majority of CL (77%) occurred at the C1-C2 level, with the subaxial cervical segments accounting for the remaining 23% of CL. Iyer et al.15 studied 120 asymptomatic adults and found the mean C2-C7 lordosis to be -12.2° (measured with the HPT method). This result is similar to the mean C2-C7 lordosis of -9.9° reported by Lee et al.16

Figure 3. Lateral cervical x-rays showing the 4 common methods for measuring cervical lordosis. A, Modified Cobb method. B, Jackson physiological stress lines. C, Harrison’s posterior tangent method. D, Ishihara index.
Janusz et al. studied 44 upright lateral cervical x-rays and compared the CL results using the mCM, the JPS method, and the HPT method. All three methods showed excellent intra- and interobserver reliability. The average C2-C7 lordosis was $-10.5^\circ \pm 13.9^\circ$, $-17.5^\circ \pm 15.6^\circ$, and $-17^\circ \pm 15.9^\circ$ for the mCM, the JPS method, and the HPT method, respectively. These results suggested that the mCM may underestimate CL. Takeshita et al. studied the relationship between the Ishihara index and C2-C7 lordosis (measured using the mCM) in 295 asymptomatic patients. The average Ishihara index was 10.9 with a standard deviation of 15.3. The average C2-C7 lordosis was $-20.3^\circ$ with a standard deviation of 14.3°. There was a highly significant correlation between the Ishihara index and CL ($r = 0.95$). However, their correlation diminished in patients with an S-shaped cervical spine, and this must be taken into consideration when dealing with cervical deformity.

It is also important to note that CL can be influenced by posture and thoracic kyphosis. Hey et al. demonstrated an average increase of CL by 3.45° from standing to sitting. In addition, CL tends to increase with age as a compensatory mechanism for the increased thoracic kyphosis and reduced lumbar lordosis to maintain the horizontal gaze.

C2-C7 SVA

Regional sagittal alignment of the cervical spine is usually measured by the C2-C7 SVA, which has been shown to correlate (albeit weakly) with health-related quality of life. The C2-C7 SVA is obtained by measuring the distance between the C2 plumb line and the vertical line drawn from the posterior superior end plate of C7 (Figure 4). Park et al. found a mean C2-C7 SVA of 4.74 mm in 80 asymptomatic patients. However, the measurements were obtained from cervical computed tomography (CT) images; thus the results are almost certainly erroneous due to the supine position. Iyer et al. reported a mean C2-C7 SVA of 21.3 mm in 120 asymptomatic patients from upright radiographs obtained from an EOS imaging system. Tang et al. retrospectively reviewed 113 patients receiving multilevel posterior cervical fusions and found that a C2-C7 SVA > 40 mm was correlated with increased disability. However, this correlation is less clear in patients undergoing laminoplasty for ossification of the posterior longitudinal ligament.

Nonetheless, from the biomechanical standpoint, increased C2-C7 SVA will increase the flexion bending moment of the cervical spine, which in turn increases the muscle energy expenditure required to keep the head erect; over time, this will likely lead to muscle fatigue, pain, and disability. However, level 1 evidence definitively proving the correlation between increased C2-C7 SVA and increased disability is still lacking, and further study on this topic is needed to further clarify the significance of C2-C7 SVA in cervical spine deformity.

Chin-Brow Vertical Angle

The CBVA is an indirect measure of horizontal gaze and can be obtained by measuring the angle subtended by the line connecting the patient’s chin to the eyebrow and the vertical line drawn from the eyebrow. This angle can be measured from clinical photographs or full-body EOS x-rays (Figure 5). The patient must be standing with hips and knee extended and the cervical spine in the neutral position. When the head is tilted down, the CBVA is positive; when the head is tilted up, the CBVA is negative; and when the head is perfectly erect and neutral, the CBVA is zero.
Iyer et al reported a mean CBVA of $-1.7^\circ$ after analyzing 120 asymptomatic adults. Lafage et al found that a CBVA between $-4.7^\circ$ and $17.7^\circ$ correlated with the lowest Oswestry Disability Index after studying a series of 303 patients. Suk et al conducted a prospective study including 34 patients with ankylosing spondylitis (AS) who had undergone pedicle subtraction osteotomy for correction of kyphotic deformity and recommended a CBVA range of $-10^\circ$ to $10^\circ$ for optimized horizontal gaze. Interestingly, a more recent study by Song et al suggested that AS patients with a postoperative CBVA between $10^\circ$ and $20^\circ$ (ie, slight flexion) had best overall results with both indoor and outdoor activities. In the experience of the senior authors (K.D.R., V.C.T.), overcorrection of cervical kyphosis can be extremely detrimental to patients’ daily activities such as cooking, walking, and toileting, where downward vision is required; a neutral CBVA at the most or a slight downward head tilt that balances appearance and function will mostly likely achieve the optimal clinical outcome.

**TIA, T1S, and Neck Tilt**

In 2012, Lee et al introduced the concept of TIA after studying lateral x-rays of 77 asymptomatic adults. This concept was analogous to the principal pelvic parameters in the lumbosacral region. The authors defined TIA as the angle subtended by the line connecting the sternum to the middle of the T1 upper end plate and the line perpendicular to the T1 upper end plate (Figure 6). Although it was originally measured on lateral x-rays, other authors found that using CT or magnetic resonance imaging may be a good alternative with better visualization of relevant structures and improved reliability. The T1S is the angle formed by the T1 upper end plate and the horizontal plane, similar to the sacral slope. The neck tilt is defined as the angle between the line connecting the sternum to the middle of the T1 upper end plate and the vertical axis, similar to the pelvic tilt.

Lee et al proposed that TIA is a fixed, morphological parameter given that the thoracic inlet is relatively immobile due to articulations between the sternum, the T1 ribs, and the T1 vertebral body. However, Janusz et al found varying TIA values depending on the position of the cervical spine (neutral, flexion vs extension) after studying 60 patients. Interestingly, Kim et al also demonstrated that the TIA values changed when the patient slept on pillows of varying heights, as well as in the sitting position. This finding further argued against the notion that the TIA is a morphological parameter that does not change with cervical motion and posture.

Oe et al conducted a study on 656 volunteers aged 50 to 89 years. The mean TIS for each decade was $32^\circ$, $31^\circ$, $33^\circ$, and $36^\circ$ for men and $28^\circ$, $29^\circ$, $32^\circ$, and $37^\circ$ for women, respectively. They found that C2-C7 SVA > 40 mm, TIS > $40^\circ$, and TIS – CL > $20^\circ$ had worse EQ-SD health status scores. Knott et al demonstrated that when the TIS was >$25^\circ$, all patients had at least 10 cm of C7-S1 SVA in a series of 52 patients. They proposed that the TIS could be useful in evaluating the overall sagittal balance. They also proposed that patients with neck tilt outside the range of $13^\circ$ to $25^\circ$ should be sent for scoliosis radiographs for a complete evaluation of their overall sagittal balance.

In recent years, there has been a trend in the subgroup of spinal surgeons who are focused on deformity to obtain 36-inch scoliosis films in all patients to assess overall sagittal balance and to aid surgical planning. This strategy has not yet been proven to be necessary. Although TIA, T1S, and neck tilt are helpful in characterization of cervical spinal deformity, their roles in surgical planning and clinical outcome are still unclear, and further investigations are required.

**Cervical Deformity Classification**

Given the paucity of high-level evidence data and relative rarity compared to other more common degenerative conditions of the cervical spine, there has not been a universally accepted classification system for cervical deformity. More importantly, it is of dubious benefit to classify cervical deformities other than with terms already in use, such as flexible, rigid, kyphotic, and scoliotic. Unlike in scoliosis, where classifications are used to determine fusion levels and research requires uniform descriptors, in the cervical spine the levels of deformity are rather obvious.

In 2015, Ames et al proposed a classification system for cervical spine deformity including a deformity descriptor plus 5 modifiers (Table). The 5 deformation descriptors include C (cervical), CT (cervicothoracic), T (thoracic), S (coronal), and...
CVJ (craniovertebral junction), which are selected based on the apex of the cervical deformity. The 5 modifiers include C2-C7 SVA, CBVA, CL Minus T1S, Myelopathy (mJOA), and SRS-Schwab classification for thoracolumbar deformity. The authors reported moderately good inter- and intraobserver reliability. However, the methodology of the study, wherein all the angular measurements were provided to the readers, makes the high reliability a foregone conclusion. The classification is therefore a work in progress; further modifications and correlation with clinical outcome are needed before it can be deemed a useful tool.

**Table. Cervical Deformity Classification System Proposed by Ames et al**

<table>
<thead>
<tr>
<th>Deformity Descriptor</th>
<th>C2-C7 SVA</th>
<th>CBVA</th>
<th>CL Minus T1S</th>
<th>Myelopathy (mJOA)</th>
<th>SRS-Schwab Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>0: &lt;4 cm</td>
<td>0: 1° to 10°</td>
<td>0: &lt;15°</td>
<td>0: 18 (none)</td>
<td>Coronal curve: T (thoracic), L (thoracolumbar or lumbar), D (double), or N (none)</td>
</tr>
<tr>
<td>CT</td>
<td>1: 4 to 8 cm</td>
<td>1: −10° to 0° or 1° to 25°</td>
<td>1: 15° to 20°</td>
<td>1: 15 to 17 (mild)</td>
<td>PI–LL mismatch: 0, +, or ++</td>
</tr>
<tr>
<td>T</td>
<td>≥8 cm</td>
<td>2: &lt;=10° or &gt;25°</td>
<td>2: &gt;20°</td>
<td>2: 12 to 14 (moderate)</td>
<td>PT: 0, +, or ++</td>
</tr>
<tr>
<td>CVJ</td>
<td></td>
<td></td>
<td></td>
<td>3: &lt;12 (severe)</td>
<td>C7-S1 SVA: 0, +, or ++</td>
</tr>
</tbody>
</table>

Abbreviations: CBVA, chin-brow vertical angle; CL, cervical lordosis; LL, lumbar lordosis; mJOA, modified Japanese Orthopedic Association score; PI, pelvic incidence; PT, pelvic tilt; SVA, sagittal vertical axis; T1S, T1 slope.

Conclusion

Cervical spine deformity is a complex problem to treat. A solid understanding of spinal biomechanics and a working knowledge of various cervical radiographic parameters are essential components in formulating a sound surgical plan that optimizes clinical outcome.

**Disclosures:** Dr Traynelis is a consultant for and a patent holder with Medtronic. He receives institutional fellowship support from Globus. Dr Riew receives royalties from Biomet and Medtronic; receives grants from AOSpine, Cerapedics, and Medtronic; and receives honoraria from North American Spine Society and AOSpine. Dr Tan has no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article.
References

Select Research Grants (2017)

Department of Neurological Sciences

**Antoaneta Balabanov, MD**
- A Randomized, Double-Blind, Placebo-Controlled, Phase 2 Study Exploring the Efficacy, Safety, and Tolerability of Natalizumab (BG00002) as Adjunctive Therapy in Adult Subjects with Drug Resistant Focal Epilepsy

**Adriana Bermeo-Ovalle, MD**
- Use of EEG in Patients with Intracerebral Hemorrhage

**Laurel Cherian, MD, MS**
- Atrial Cardiopathy and Antithrombotic Drugs in Prevention after Cryptogenic Stroke

**Cynthia Comella, MD**
- A Phase 3, Randomized, Double-Blind, Placebo-Controlled, Parallel Group, Multicenter Trial to Evaluate the Efficacy and Safety of a Single Treatment of DaxibotulinumtoxinA for Injection in Adults with Isolated Cervical Dystonia
- A Phase 3, Multicenter, Randomized, D-B, Placebo-Controlled Study with an Open-Label Phase to Determine the Efficacy and Safety of Tozadenant as Adjunct Therapy in Levodopa-Treated Patients with PD Experiencing End of Dose “Wearing-Off”
- A Phase 2, Open-Label, Dose-Escalating Study to Evaluate the Safety and Preliminary Efficacy of RTT150 for Injection in Isolated Cervical Dystonia
- An Open-Label, Multicenter, Double-Blind Study to Evaluate the Safety and Tolerability of Perampanel (E2007) in Subjects with Cervical Dystonia (SAFE-Per CD)
- RE-024 for the Treatment of Pantothenate Kinase-Associated Neurodegeneration

**James Conners, MD, MS**
- Platelet-Oriented Inhibition in New TIA and Minor Ischemic Stroke (POINT) Trial
- ARAMIS: Addressing Real World Anticoagulant Management Issues in Stroke

**Rima Dafer, MD**
- A Phase 1b/2, Multicenter, Double-Blind (Principal Investigators and Study Subjects Blinded, Sponsor Unblinded), Placebo-Controlled, Randomized, Single-Ascending Dose Study to Assess the Safety, Pharmacokinetics, and Pharmacodynamics of DS-1040b in Subjects with Acute Ischemic Stroke

**Jori Fleisher, MD**
- Reaching the Most Vulnerable: A Novel Model of Care in Advanced Parkinson’s Disease
- Care Where It Counts: Interdisciplinary Home Visits for PSP-Related Disorders

**Christopher Goetz, MD**
- Management of Parkinson’s Disease Psychosis in Actual Practice
- A Randomized, Double-Blind, Placebo-Controlled Trial of Urate-Elevating Inosine Treatment to Slow Clinical Decline in Early Parkinson Disease
- A Phase 3, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study to Examine the Efficacy, Safety and Tolerability of APL-130277 in Levodopa Responsive Patients with Parkinson’s Disease Complicated by Motor Fluctuations (“OFF” Episodes)
- A Phase III, Multicenter, Randomized, Double-Blind, Double-Dummy, Active-Controlled Study Comparing the Efficacy and Safety of Gastric Retentive, Controlled Release Accordion Pill™ Carbipoda/Levoli Fluctuating PD Patients
- An Open-Label, Phase 3 Study Examining The Long-Term Safety, Tolerability and Efficacy of APL-130277 in Levodopa Responsive Patients with Parkinson’s Disease Complicated by Motor Fluctuations (“OFF” Episodes)
- An Open-Level, Multicenter, Follow-Up Study Designed to Evaluate the Long-Term Effects of AP-CD/LD in Fluctuating Parkinson’s Disease Subjects Who Completed Study IN 11 004
Jennifer Goldman, MD, MS

- Study of 5-HT6/5-HT2A in the SYNAPSE Parkinson's Disease Dementia Trial
- Evaluation of the Parkinson's Disease Psychosis Virtual Reality Simulator Experience
- A Phase 2b, Double-Blind, Randomized, Placebo-Controlled Study of RVT-101 in Subjects with Dementia with Lewy bodies (DLB)
- Mild Cognitive Impairment and Endurance Exercise in Parkinson's Disease
- Serotonin Gene Polymorphisms (5-HT6 and 5-HT2A) and Parkinson's Disease Cognitive Impairment
- Effect of LY3154207 on Cognition in Mild to Moderate Parkinson's Disease Dementia
- A Multicenter, Randomized, Double-Blind, Placebo-Controlled Study of the Safety, Pharmacokinetics and Pharmacodynamics of B11B054 in Subjects with Parkinson's Disease

Deborah A. Hall, MD, PhD

- A 12-Month, Dose-Level Blinded Study Investigating the Safety and Efficacy of CVT 301 (Levodopa Inhalation Powder) in Parkinson's Disease Patients with Motor Response Fluctuations (OFF Phenomena)
- A Randomized, Double-Blind, Placebo-Controlled Multiple Dose Study to Assess Efficacy, Safety, Tolerability, and Pharmacokinetics of ABBV-8E12 in Progressive Supranuclear Palsy
- A Phase 2A, Double-Blind, Placebo-Controlled, Randomized Withdrawal Study Evaluating the Efficacy, Safety, Tolerability, and Pharmacokinetics of SAGE-217 in the Treatment of Subjects with Essential Tremor (ET)
- A Phase 3, Randomized, Double-Blind, Placebo-Controlled Study Investigating the Efficacy and Safety of CVT-301 (Levodopa Inhalation Powder) in Patients with Motor Response Fluctuations (OFF Phenomena)
- Care, Research, and Unmet Needs for African Americans with Parkinson's Disease in Chicago
- A randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study to Evaluate the Efficacy and Safety of Intravenously Administered B11B092 in Participants with Progressive Supranuclear Palsy

Michael Y. Ko, MD

- Biogen STRIVE 101MS407 A Phase 4, Multicenter, Observational, Open-Label, Single-Arm Study of Tysabri in Early RRMS in Anti-JCV Ab Negative Patients

Aikaterini Kompoliti, MD

- A Phase 3, Double-Blind, Placebo-Controlled, Parallel Group Study of Isradapine as a Disease Modifying Agent in Patients with Early Parkinson’s Disease/ Steady- PD3
- A Randomized, Double-Blind, Placebo Controlled Study of SD-809 (Dutetrabenazine) for the Treatment of Moderate to Severe Tardive Dyskinesia
- An Open-Label, Long-Term Safety Study of SD-809 (Dutetrabe Nazine) for the Treatment of Moderate to Severe Tardive Dyskinesia
- A Randomized, Double-Blind, Placebo-Controlled Study to Assess the Safety and Efficacy of NBI-98854 in Adult Subject with Tourette Syndrome/Protocol No. NBI-98854-1505
- A Clinical Study Of Patients with Symptomatic Neurogenic Orthostatic Hypotension To Assess Sustained Effects Of Droxidopa Therapy
- An Open-Label, Safety and Tolerability Study of NBI-98854 for the Treatment of Subjects with Tourette Syndrome
- A Phase 3, 12-Week, Multicenter, Multinational, Randomized, DB, DD, Parallel Group Study to Determine the Efficacy, Safety, and Tolerability of P2B001 Once Daily Compared to Its Individual Components in Early PD and to a Calibration Arm

Igor Koralnik, MD

- Role of Inflammation in Progressive Multifocal Leukoencephalopathy
- Virus Detection in Patients with Neurological Disorders and Infections
- Epidemiological Studies in Patients with Neurologic Disorders
- Role of Inflammation in Progressive Multifocal Leukoencephalopathy
- Cohort of HIV-Associated Seizures and Epilepsy in Zambia (CHASE): Scale Up and Expansion Informed by R21 Findings
- Cellular Auto-Immune Mechanisms of Narcolepsy
- JC Virus Infection of Choroid Plexi and Meninges of Patients with PML, JCV, GCN, JCVE, and Control Subjects
- Pathogenesis of a JC Virus Variant in Pyramidal Neurons
Jeffrey Kordower, PhD

• Developing a Human Es Cell Derived Dopamine Neuron Source for Cell Therapy in Parkinson's Disease
• Evaluation of Alpha-Synuclein Immunohistochemical Methods for the Detection of Lewy-Type of Synucleinopathy in Gastrointestinal Biopsies
• Transplantation of Cryopreserved iPSC-Derived Dopamine Neurons for Parkinson's Disease
• Nortriptyline-Mediated Attenuation of Alpha-Synuclein Pathology in Parkinson's Disease
• RnaI Therapy for Spinocerebellar Ataxia Type 1
• Human iPSC-Based Personalized Cell Therapy of PD

George Lopez, MD

• INTREPID: Impact of Fever Prevention in Brain Injured Patients
• ESCAPE- NA1: A Multicenter, Randomized, Double-Blinded, Placebo-Controlled, Parallel Group, Single-Dose Design to Determine the Efficacy and Safety of Intravenous NA-1 in Subjects with Acute Ischemic Stroke Undergoing Endovascular Thrombectomy
• Phase I/2a, Multicenter, Controlled, Randomized, Open-Label, Dose Escalation, Safety, Tolerability, and Pharmacokinetic Study Comparing the EG-1962 and Nimodipine in Patients with Aneurysmal Subarachnoid Hemorrhage
• iDEF Trial (Futility Study of Deferoxamine Mesylate in Intracerebral Hemorrhage
• A Phase 3, Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Efficacy and Safety Study Comparing EG-1962 to Standard of Care Oral Nimodipine in Adults with Aneurysmal Subarachnoid Hemorrhage
• ASTROH Aneurysmal Subarachnoid Hemorrhage Trial Randomizing Heparin

Rabia Malik, MD

• A Phase 2, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Safety, Tolerability, and Preliminary Efficacy of RA101495 in Subjects with Generalized Myasthenia Gravis

Daniel A. Nicholson, PhD

• Computational Neurobiology of Hippocampal Dendrites
• Proteomic Reconstructive Microscopy of Healthy and Diseased Dendrites

Rebecca O'Dwyer, MD

• Multicenter, Open-Label, Randomized, Parallel-Group, Active-Controlled Study to Assess the Efficacy and Safety of Brivaracetam Administered Intravenously as Treatment for Increased Seizure Activity in an Epilepsy Monitoring Unit Setting
• Phase IV Multicenter Open Label Study of Efficacy and Safety of Eslicarbazepine Acetate as First Add-On to Levetiracetam or Lamotrigine Monotherapy or as Later Adjunctive Treatment for Subjects with Uncontrolled Partial-Onset Seizures
• Microburst VNS Therapy Feasibility Study in Subjects with Refractory Epilepsy

Kalipada Pahan, PhD

• Characterizing Novel Hippocampal Drugs for Alzheimer's Disease
• Identifying Novel PPAR Ligands from Cerebellum
• Dose Reporting Study of Gemfibrozil and Vitamin A Following Oral Administration to Cin2 (+/-) Mice
• PPAR-Alpha in App Metabolism

Gian Pal, MD

• Parkinson's Disease and DBS: Cognitive Effects In GBA Mutation Carriers
• A randomized, DB, P-C, Phase Ila, Parallel Group, Two-Cohort Study to Define the Safety, Tolerability, Clinical, and Exploratory
• Multicenter, Randomized, Double-Blind, Placebo-Controlled Study to Assess the Efficacy, Safety, Pharmacokinetics, and Pharmacodynamics of GZ/SAR402671 in Patients with Early-Stage Parkinson’s Disease Carrying a GBA Mutation or Other Pre-Specified Variant

Clement Pillainayagam, MD

• A071101: A Phase II Randomized Trial Comparing the Efficacy of Heat Shock Protein-Peptide Complex-96 (HSPPC-96) Vaccine Given with Bevacizumab Versus Bevacizumab Alone in the Treatment of Surgically Resectable Recurrent Glioblastoma Multiforme (GBM)
• A Phase II/III Randomized Trial of Veliparib or Placebo in Combination with Adjuvant Temozolomide in Newly Diagnosed Glioblastoma with MGMT Promoter Hypermethylation
Sebastian Pollandt, MD
• A Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of Sage-547 Injection in the Treatment of Subjects with Super-Refractory Status Epilepticus

Lubov Romantseva, MD
• A Multicenter, Double-Blind, Randomized, Placebo-Controlled Trial with an Open-Label Extension Phase of Perampanel as Adjunctive Treatment in Subjects at Least 2 Years of Age with Inadequately Controlled Seizures Associated with Lennox-Gastaut Syndrome

Marvin Rossi, MD, PhD
• Developing an ‘Activation Function-Dependent’ Intra-Operative Depth Lead Guidance System for Direct Neuromodulation Therapy in Patients with Refractory Focal-Onset Epilepsy: A BodyTom CT and O-Arm Comparison
• Interfacing a Mobile Health Delivery Model for Rural Patients with Refractory Epilepsy
• Interfacing a Mobile Health Delivery Model for Pediatric Patients with Refractory Epilepsy
• RNS System Post-Approval Study in Epilepsy

Sarah Song, MD, MPH
• MyRIAD: Mechanisms of Early Recurrence in Intracranial Atherosclerotic Disease
• PRISMS: A Phase IIIb, Double-Blind, Multicenter Study to Evaluate the Efficacy and Safety of Alteplase in Patients with Mild Stroke: Rapidly Improving Symptoms, and Minor Neurological Deficits

Dusan Stefoski, MD
• A Multicenter, Randomized, Double-Blind, Parallel-Group, Placebo-Controlled Variable Treatment Duration Study Evaluating the Efficacy and Safety of Siponimod (Baf312) in Patients with Secondary Progressive Multiple Sclerosis
• A Randomized, Double-Blind, Double-Dummy, Parallel-Group Study Comparing the Efficacy and Safety of Ofatumumab versus Teriflunomide in Patients with Relapsing Multiple Sclerosis
• A Multicenter, Double-Blind, Placebo-Controlled Study in Subjects with Relapsing Multiple Sclerosis to Evaluate the Efficacy and Safety of BIIB033 as an Add-on Therapy to Anti-Inflammatory Disease-Modifying Therapies

Leonard Verhagen Metman, MD, PhD
• Effect of Unilateral and Bilateral STN Stimulation on Eye-Hand Coordination
• Product Surveillance Registry Base Protocol
• A 15-Week, Phase 2, Double-Blind, Randomized, Placebo-Controlled, Dose Ranging Study to investigate the Efficacy, Safety, and Tolerability of PF-06649751 in Subjects with Motor Fluctuations Due to Parkinson’s Disease
• A Phase II, Double-blind, Placebo-Controlled, Crossover Study to Assess Clinical Benefit and Safety of Droxidopa in the Treatment of Parkinson’s Disease
• Post-Market Clinical Follow-Up Evaluating the Infinity Deep Brain Stimulation Implantable Pulse Generator System (PROGRESS STUDY)

Department of Neurological Surgery

Richard Byrne, MD
• A Retrospective Review of Meningioma Surgery Clinical Outcomes
• A Retrospective Review on Cortical Stimulation Mapping Techniques in Brain Tumor Patients
• Schwepp Grant for Dual Label Fluorescence Imaging of Brain Tumors
• Temporal Lobectomy, Memory, Sleep, and Dreams

Michael Chen, MD
• PHIL: Study of PHIL® Embolic System in the Treatment of Intracranial Dural Arteriovenous Fistulas
• STERLING: A Prospective, Multicenter, Single-Arm Study to Obtain “Real World” Clinical Data and Characterize the Acute and Long-Term Performance of Micrusframe and Galaxy Coils for the Endovascular Treatment of Intracranial Aneurysms
• Feasibility and Limitations of Automated Computed Tomography Perfusion Imaging in Clinical Practice
• Post-Aneurysm SAH Memory Loss
• PREMIER: Prospective Study on Embolization of Intracranial Aneurysms with Pipeline Embolization Device
• BARREL: Prospective, Multicenter, Single-Arm Study of the Reverse Medical Barrel Vascular Reconstruction Device (VRD) for Adjunctive Treatment to Embolic Coils for Wide-Neck, Intracranial, Bifurcating/Branching Aneurysms of Middle Cerebral and Basilar Arteries
• SCENT: The Surpass Intracranial Aneurysm Embolization System Pivotal Trial to Treat Large or Giant Wide-Neck Aneurysms
• WEB-IT: The WEB Intrasaccular Therapy Study
R. Webster Crowley, MD

- NAPA: A Prospective, Multicenter, Single-Arm Study to Evaluate the Safety and Effectiveness of the PulseRider Aneurysm Neck Reconstruction Device Used with Endovascular Coil Embolization in the Treatment of Wide-Neck Bifurcation Intracranial Aneurysms
- OPEN-UP: Operative Procedures versus Endovascular Neurosurgery for Untreated Pseudotumor Trial
- ENRICH: Early Minimally-Invasive Removal of ICH
- ENRICH AI: Automated Detection, Characterization, Triage, and Recruitment of ICH Subjects Using Artificial Intelligence in the ENRICH Trial
- ATLAS: Safety and Effectiveness of the Treatment of Wide-Neck, Saccular Intracranial Aneurysms with the Neuroform Atlas™ Stent System

Harel Deustch, MD

- Oxiplex Adhesion Barrier Gel
- A Concurrently Controlled Study of the LimiFlex Paraspinous Tension Band in the Treatment of Lumbar Degenerative Spondylolisthesis with Spinal Stenosis
- LIFT: Lumbar Interbody Fusion Trial
- STRIVE: A Phase 2b, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Safety and Efficacy of Staphylococcus Aureus 4-Antigen Vaccine (SA4Ag) in Adults Undergoing Elective Open Posterior Spinal Fusion Procedures with Multilevel Instrumentation

Richard Fessler, MD, PhD

- Expectations and Outcomes: MIS vs. Open
- Radiographic Findings After Anterior Cervical Discectomy and Fusion with Translational and Rigid Plating System
- Prospective, Multicenter Minimally Invasive Adult Spinal Deformity Outcomes Database Registry
- Asterias Stem Cell Treatment for SCI: Long-Term Follow-Up

John O'Toole, MD, MS

- ASPIRE: An Assessment of P-15L Bone Graft in Transforaminal Lumbar interbody fusion (TLIF) surgery
- MTRON: Metastatic Tumor Research and Outcome Network

Sepehr Sani, MD

- INTREPID
- MEP: Motor Evoked Potentials in Current Steering and Ring Mode Stimulation
- Reclaim DBS for Obsessive Compulsive Disorder (OCD) Therapy

Vincent Traynelis, MD

- Critical Analysis of Tracheoesophageal Bundle Retraction Force Pre- and Post-Section of the Omohyoid Muscle During Anterior Cervical Spine Surgery
- Assessment of Peri-Operative Morbidity and Mortality Following Anterior-Posterior Cervical Spine Decompression and Fusion
- Machined Cervical Interfacet Allograft Spacers in Atlanto-Axial Instability
- Hyperlordotic Cornerstone Graft Study
Volume and Quality Data

Volumes, neurology and neurological surgery

Neurology volumes*, fiscal years 2012-2018

Neurology outpatient visits, fiscal years 2012-2018

Neurological surgery outpatient visits, fiscal years 2012-2018

Volume of patients monitored for epilepsy, calendar years 2012-2018

Neurological surgery volume of major cases by area, fiscal year 2018

Rush had the highest volume of neurosurgical discharges in the Chicago region for fiscal years 2011-2018.
Mortality, neurology and neurological surgery

Neurological surgery mortality (observed/expected), fiscal years 2012-2018

Source: UHC

Quality indicators, stroke

Median times to endovascular recanalization treatment at Rush, fiscal year 2017

Sources: Get With the Guidelines and internal data

1Includes all comprehensive stroke centers participating in Get With the Guidelines stroke data registry

2Includes all US hospitals participating in Get With the Guidelines stroke data registry

Stroke case volumes, fiscal year 2017

Total: 1059 Cases

<table>
<thead>
<tr>
<th>Category</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischemic stroke</td>
<td>646</td>
</tr>
<tr>
<td>Transient ischemic attack (&lt;24 hours)</td>
<td>78</td>
</tr>
<tr>
<td>Subarachnoid hemorrhage</td>
<td>90</td>
</tr>
<tr>
<td>Intracerebral hemorrhage</td>
<td>245</td>
</tr>
</tbody>
</table>

61% 7% 9% 23%
Changing Minds

Like many people, David Bennett, MD, is concerned about Alzheimer’s disease, which currently afflicts an estimated 5.7 million people in the United States and is projected to develop in 14 million people in the U.S. by 2050.

Unlike most people, Bennett someday may be able to stop it.

The director of the Rush Alzheimer’s Disease Center (RADC) at Rush University Medical Center, Bennett is one of the world’s foremost Alzheimer’s disease researchers. In recognition of his accomplishments, in 2018 he was chosen to receive the highest honor in the world for dementia research, the Potamkin Prize for Research in Pick’s, Alzheimer’s and Related Diseases, by the American Academy of Neurology and the American Brain Foundation.

He received the award on April 22 at the AAN’s annual conference in Los Angeles. It’s a sign of his stature that when Bennett told the organizer of a conference in China he would have to cancel a planned talk there to be on hand to receive the award, she rescheduled the conference around his availability.

Bennett—who also is the Robert C. Borwell Professor of Neurological Science at Rush Medical College—has been pursuing a solution to Alzheimer’s disease, the leading cause of dementia, since the early 1990s. He currently is the primary investigator of 8 different studies funded by the National Institutes of Health, and a co-investigator on more than a dozen others. (He also serves on several National Institutes of Aging committees, including the National Advisory Council on Aging.)

He’s building on his quarter century of research discoveries to identify specific proteins in the body that affect the development of Alzheimer’s disease, so that he and other researchers can design treatments that target those proteins and prevent Alzheimer’s from occurring.
“As a public health strategy, we have to prevent the disease. However, people have it and will continue to get it, so we also need to develop better treatments.”

**Building a repository of data—and brains**

“It’s a terrible disease,” says Bennett, who has been caring for Alzheimer’s patients and their families for more than 30 years. “Of all the things that happen to older people, the number one thing the vast majority wants to prevent is the loss of cognition. They don’t want to lose their ability to plan for the future and their ability to remember the past, the things they’ve done, and the people they love.”

The human brain has an extraordinary ability to rearrange neural connections as it learns and adapts to disease and injury. By the time Alzheimer’s dementia overwhelms that ability and begins robbing people of their thoughts and memories, the damage it has caused is so great that it has thwarted massive efforts to find a cure. “Between 1993 and 2002, 5 drugs were (FDA) approved for the symptomatic treatment of Alzheimer’s disease, and they don’t work very well,” Bennett says. No new drug treatments for Alzheimer’s have been approved since then.

“As a public health strategy, we have to prevent the disease,” he says. “However, people have it and will continue to get it, so we also need to develop better treatments.”

Bennett and his colleagues started and lead 2 ongoing studies funded by the National Institutes of Health—the Religious Orders Study, which examines memory loss in Catholic nuns, priests and brothers from across the United States; and the Rush Memory and Aging Project, which is a similar study of laypeople in northeastern Illinois. Since they began testing participants in 1994 and 1997 respectively, the 2 studies between them have enrolled more than 3,500 older people to date and continue to recruit participants.

Participants do not have dementia when they enroll in the studies, but some develop it over time. The studies annually collect clinical information (including brain imaging) and biospecimens (blood, etc.) from the participants. The annual detailed data collection for nearly a quarter century makes these studies unique.

Even more noteworthy is that all participants agree when they enroll in either study to donate their brains for research after their deaths. Participants who are autopsied at Rush also donate spinal cords, nerves, and muscle for studies of gait and balance.

“These are the only 2 studies in the world of risk factor for Alzheimer’s dementia in which all participants are brain donors,” Bennett says. More than 1,500 deceased participants have donated their brains so far, with more coming every year.

By comparing the pathology (anatomical damage) in the brain samples of people who did and did not develop Alzheimer’s dementia with the clinical data recorded during their lives, and examining what causes these changes,
statisticians, neuropsychologists, epidemiologists, physicists, and biomedical engineers. They work closely with a community engagement team, managers, coordinators, field and laboratory technicians, information systems analysts, and administrators.

In addition to drawing on the 2 studies for its own research, the RADC shares the data and biospecimens from these studies with researchers around the world to advance the development of therapies to treat and prevent memory loss and dementia. “The resources that we generate here are extraordinary and unique,” Bennett says. “They don’t exist anywhere else in the world.

Bennett was only 33 years old when the National Institute on Aging funded the Rush Alzheimer’s Disease Center in 1991. “The one thing you have to have for what I do is patience,” he says. “I don’t think I could have done this anywhere else. Rush’s support has allowed us to take these long view arcs that are almost impossible to achieve at other institutions.”

Understanding the role of diversity

The risks for Alzheimer’s disease, and most likely the solutions for it as well, differ greatly among ethnic groups, and researchers need to understand those differences. However, many black individuals and Latinos are reticent to donate their brains for study after their deaths due to cultural sensitivities. Of the 1,500 donated brains at Rush, only about 40 are from black study participants and another 40 are from Latinos. There are another 35 from 3 other cohort studies conducted by the RADC. “It will take many more years to achieve sufficient numbers to conduct the kind of work in minorities being done with the donations from whites,” Bennett says.

However, colleagues at the RADC are also following two cohorts of older African Americans and one of Latinos. The other studies follow similar methods, except brain donation is optional. As these studies mature, Bennett and his colleagues will be in a unique position to extend their work to these diverse and understudied older persons.

Groundbreaking insights into the disease

The first wave of published research papers that Bennett and his colleagues at the RADC produced, from 1994 to 2008, focused on risk factors for Alzheimer’s dementia and the neurobiology of the illness. “This thing we call clinical Alzheimer’s dementia is an extraordinarily complex set of different factors going on in your brain,” Bennett says. “Some factors are driving you to lose memory, and other factors are helping protect you. They include experiential, psychological, and medical risk factors, in addition to multiple neuropathologies and resilience factors in the brain.”

Bennett’s group was the first to identify many of the factors that increase or reduce the risk of Alzheimer’s disease dementia. Just a few of the many discoveries they have published include that more cognitive activity is associated with a reduced risk of Alzheimer’s dementia; that more purpose in life is associated with a reduced risk; that psychological risk factors, such as neuroticism, depressive symptoms, and loneliness, are associated with an elevated risk; and that diabetes likewise is a risk factor.

Defining the role of pathology in dementia

Alzheimer’s disease produces pathology—physical damage—in the brain, such as blood vessel disease in the form of cerebral amyloid angiopathy, or the buildup of harmful proteins known as amyloid plaques between brain cells and neurofibrillary tangles within brain cells. Because everyone in the 2 long-term Rush studies is an organ donor, the RADC has an unprecedented opportunity to examine how the wide range of risk factors is related to brain pathology.

A colleague of Bennett’s on the RADC team was the first to report that mixed pathologies are the most common cause of Alzheimer’s dementia in older people. On the other hand,
one of the biggest discoveries that Bennett and his colleagues have made is that brain pathology doesn’t mainly determine whether or not a person becomes demented, and how far dementia progresses. They were also the first to report that people without any cognitive impairment whatsoever often develop brain pathologies. This work contributed to the evolution of new criteria for Alzheimer’s disease adopted by the field in 2011 and again in 2018.

“You can get a brain full of pathologies without losing much cognition, or you can have very little pathology and suffer from severe loss of cognition,” Bennett says. “We’ve found numerous risk factors for cognitive decline and dementia that aren’t related to any brain pathology. Those risk factors are doing something, but it’s not causing any pathology that we know of today.”

These findings date back to 2003, when Bennett and his colleagues published the first research paper that combined risk factors with pathology and cognitive decline in the same model. In this paper, the risk factor was the ApoE4 gene, which does clearly cause the development of Alzheimer’s pathology.

In subsequent papers that they’ve continued to publish to this day, however, the researchers have reported that while they could correlate a risk factor with cognitive decline and the development of dementia, they couldn’t match the risk factor with brain pathology. “That means that there are systems in the brain that determine whether or not you lose cognition completely separate from the development of known brain pathologies,” Bennett says. “There probably aren’t a lot of them, and the question is, ‘How do we find them?’”

**Targeting resilience to counter brain disease**

Resilience is the term Bennett and his colleagues use to refer to cognitive change that cannot be explained by common brain pathologies such as plaques and neurofibrillary tangles. A person may be more or less resilient, resulting in slower or faster loss of cognition.

Bennett wants to know why some people are more resilient, others are less, and how to increase resilience in everyone. He thinks that resilience could be an approach to therapy that could prevent loss of cognition from all common brain diseases, of which there are more than a dozen and counting, including Alzheimer’s disease. “Resilience doesn’t care what brain pathology or injury is developing,” Bennett says. “All people have some resilience. It’s just that some have more and others less. If you can augment it, you can actually counter the effects of multiple different brain diseases.” That includes Parkinson’s disease and stroke, in addition to Alzheimer’s disease.

Therefore, Bennett and his colleagues are focusing their work on identifying targets—factors that affect resilience—and trying to determine if they’re “drug-able”: that is, if they can be affected by a medication that eventually could be used in human beings. In fact, it’s been his long-term goal since the late 1990s. Bennett expects most of these therapeutic targets to be proteins in the brain that will be found to be associated with a faster or slower rate of memory loss, and a higher or a lower risk of Alzheimer’s disease. “Then we’ll try and move them in the direction of a healthier level of the protein and hope that it will improve people’s cognition,” he explains.

**Creating “cognition in a dish”**

Working with colleagues at Columbia, Harvard, and Pacific Northwest National Laboratories, his team has already identified two such proteins, known as Ak4 and ITPK1, which are associated with memory loss despite not being related to any brain pathology. The association is with higher levels of Ak4 and lower levels of ITPK1, so blocking the former and raising levels of the latter may increase resilience and help maintain cognition.

“These are the first 2 and the strongest ones we have found to date. There’ll be a lot more,” Bennett says. “The reason we’re interested in proteins is that proteins are the most common target for therapeutics. We’ve identified targets for
“For a long time it wasn’t really clear how we were going to get to that therapeutic pipeline. I’m not saying we’re going to get there any time soon, but at least the roadmap that we need to follow has become very, very clear.”

resilience, but to see if the targets are drug-able, I need to put them in some kind of high throughput model. I basically need cognition in a dish.”

Therefore, Bennett’s team is taking tissues donated by participants in the 2 long-term Rush studies, extracting blood and skin cells and reverse engineering them back to being pluripotent stem cells, which can develop into any kind of cell in the body. Then they’re stimulating these cells to become different types of brain cells that can be studied in a laboratory dish.

He’s developing these cells from tissue taken from deceased participants whose medical history he knows well, including knowing how resilient they were when they were alive. “The question is, can we develop a method of challenging those cells and measure something that correlates with the known resilience?” Bennett asks. In other words, he and his team want to find a way to mimic resilience in the cells growing in the dish. Since the cells came from the deceased participants, they can match what is found in the dish with what is known about the participant.

“When we have a proxy for resilience in a dish, then we can take the cells and manipulate genes that affect the production of Ak4 and ITPK1 and other proteins to see if we affect resilience in the desired direction,” Bennett says. “What we’re talking about now was science fiction when we started. It’s science fiction even to a lot of my colleagues today.”

**Seeing the light**

If he can make what once was science fiction a reality, Bennett then could move on to similar experiments in flies and mice that would be precursors to possible clinical trials of the intervention in human patients. In theory, the interventions would alter the levels of multiple proteins identified as Alzheimer’s risk factors, up or down as needed to increase resilience.

The therapy wouldn’t be limited to people with levels of those proteins that put them at Alzheimer’s risk. “The interventions are for everyone,” Bennett says, because even people with protective levels of a given protein might benefit from more protection.

“This has been the culmination of over 2 decades worth of work,” he says. “What excites me is that for a long time it wasn’t really clear how we were going to get to that therapeutic pipeline, but over the last 5 years it has become very clear in my mind. The technology has been developed, we have the resources here at the Rush Alzheimer’s Disease Center, a remarkable team of scientists not only here but across the country and around the world, and we are finally moving into the realm where we can actually see the light at the end of this tunnel. I’m not saying we’re going to get there any time soon, but at least the roadmap that we need to follow has become very, very clear. It’s very exciting, and I hope I’m around long enough to see those drugs come out and be helping people.”

❉
For a patient consultation or referral to a neurologist at Rush, please call (312) 942-4500. For a neurosurgeon at Rush, call (312) 942-6644.
PLEASE NOTE: All physicians featured in this publication are on the medical faculty of Rush University Medical Center. Some of the physicians featured are in private practice and, as independent practitioners, are not agents or employees of Rush University Medical Center.

Photography by Eric Herzog and the Rush Production Group